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Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, November 15-18

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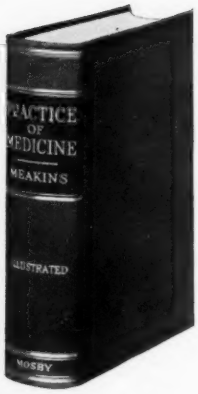

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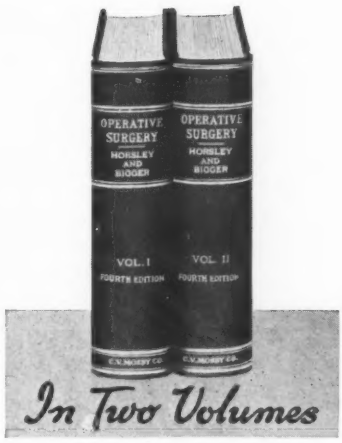

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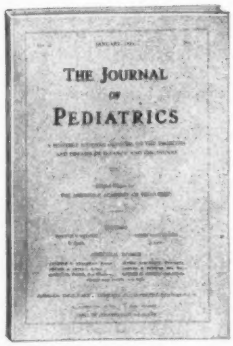

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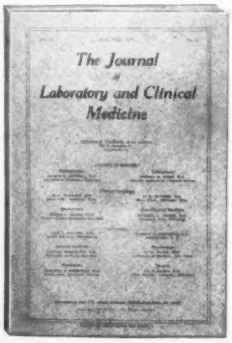

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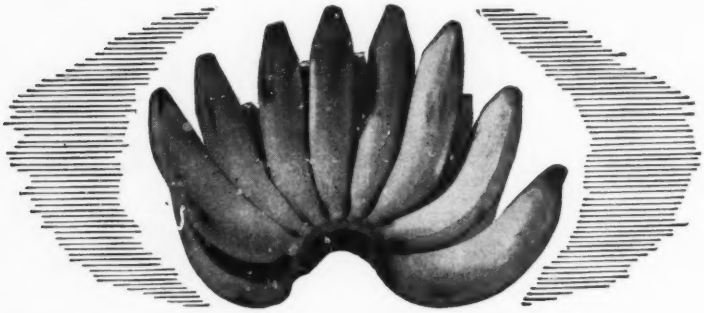

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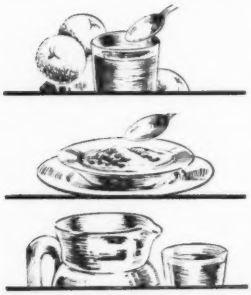

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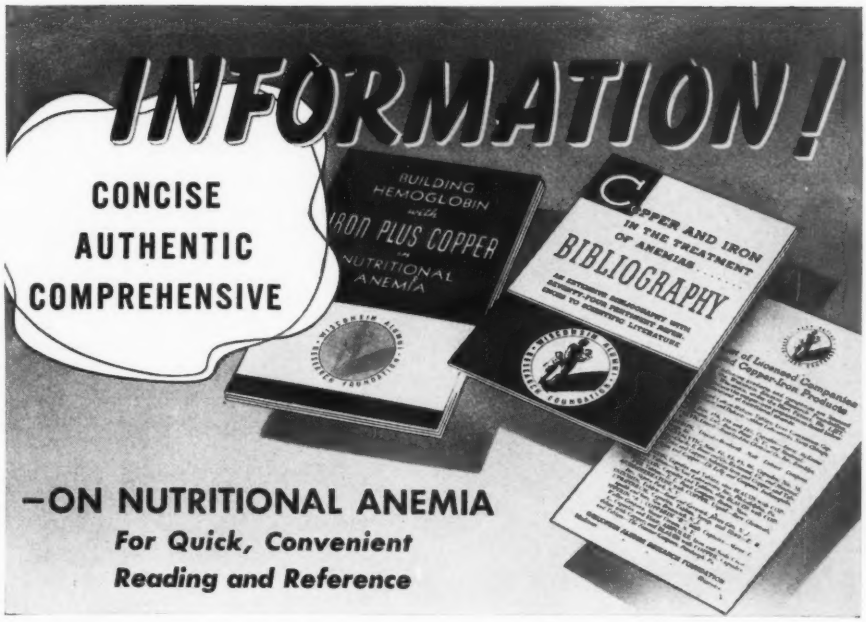

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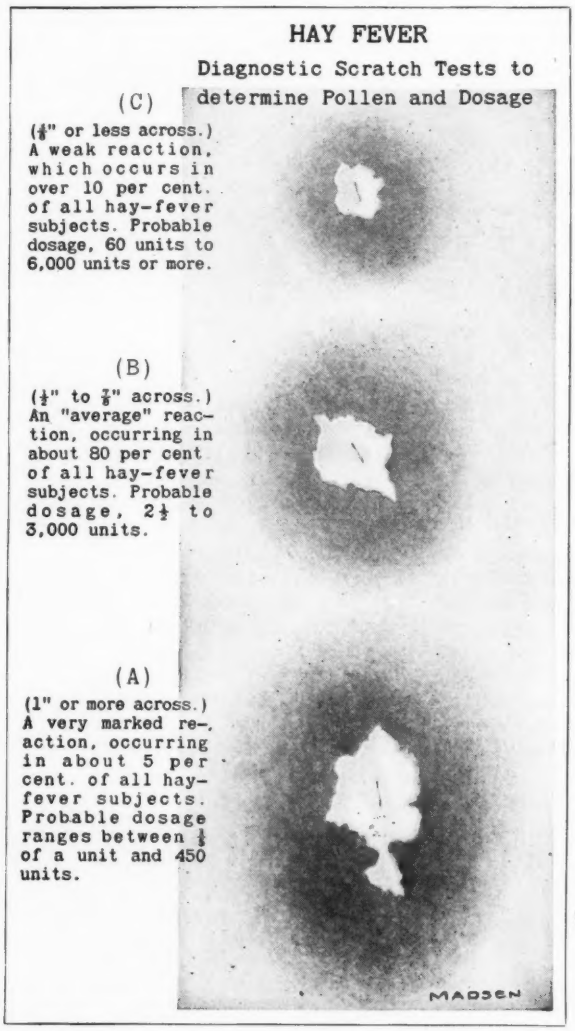
THE INCIDENCE OF HAY FEVER has been variously estimated as between 1 and 2 per cent. of the population of the United States. Some recent estimates are even higher. Thus there are about two million hay fever sufferers in this country.


HAY FEVER
Diagnostic Scratch Tests to determine Pollen and Dosage
(C)
(⅛" or less across.) A weak reaction, which occurs in over 10 per cent. of all hay-fever subjects. Probable dosage, 60 units to 6,000 units or more.
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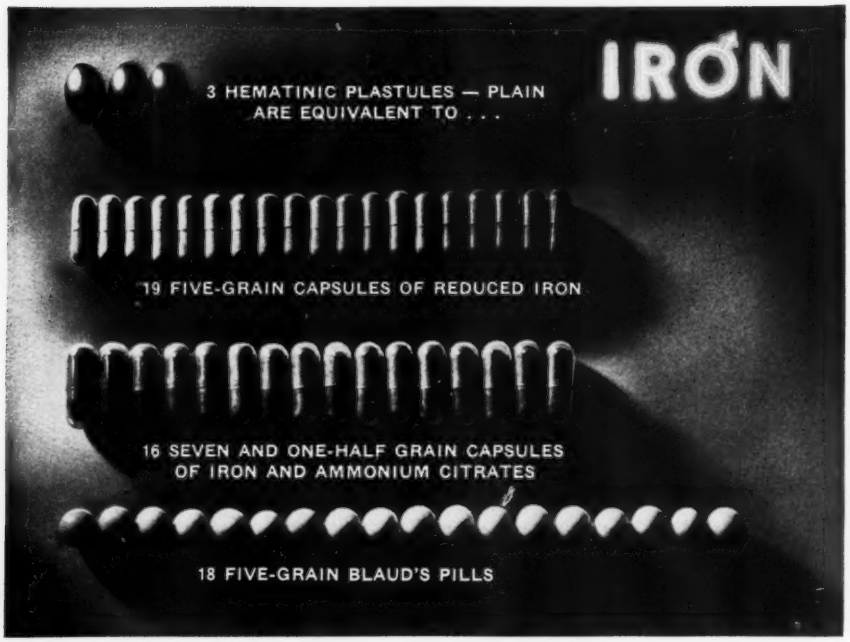
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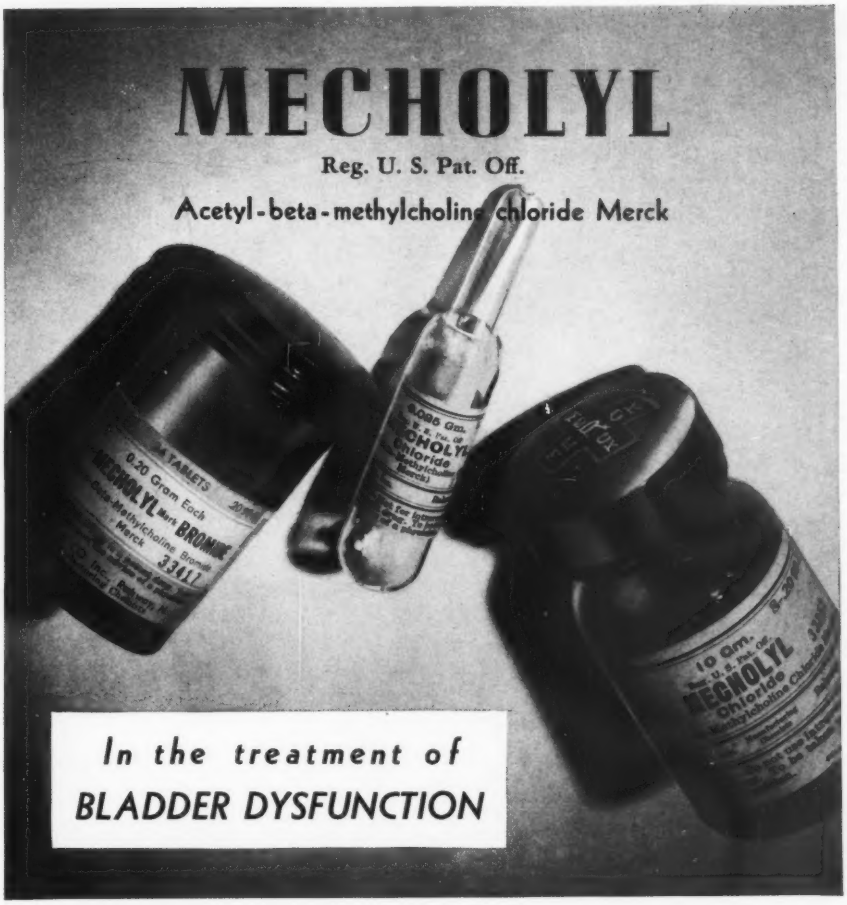

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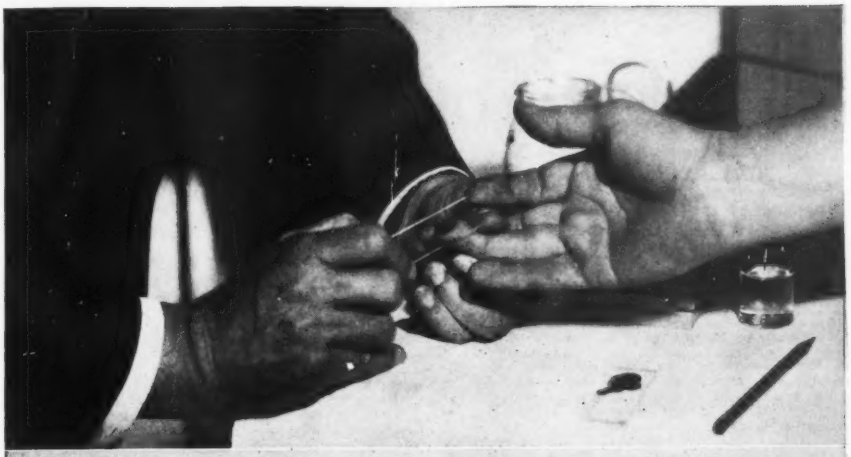

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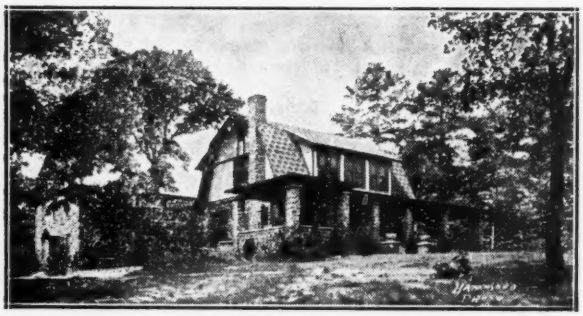

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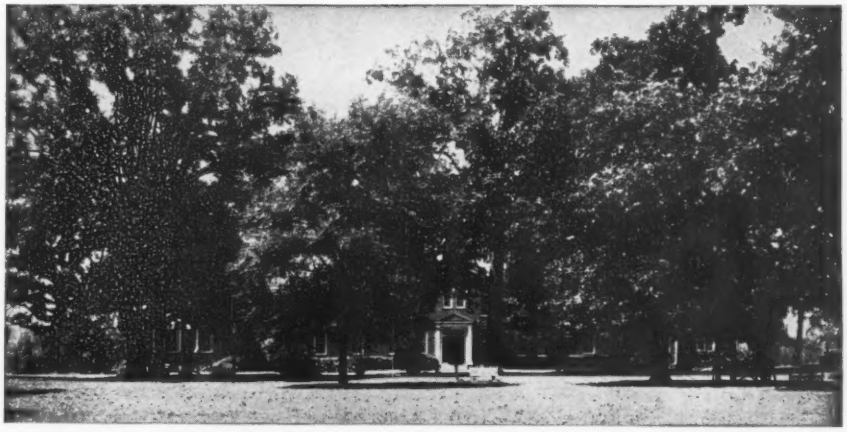

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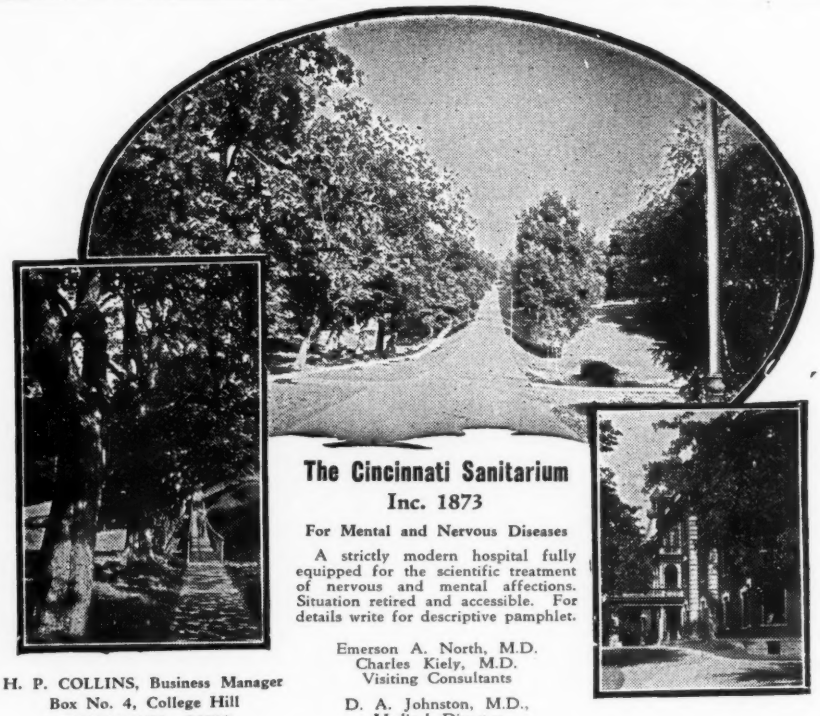

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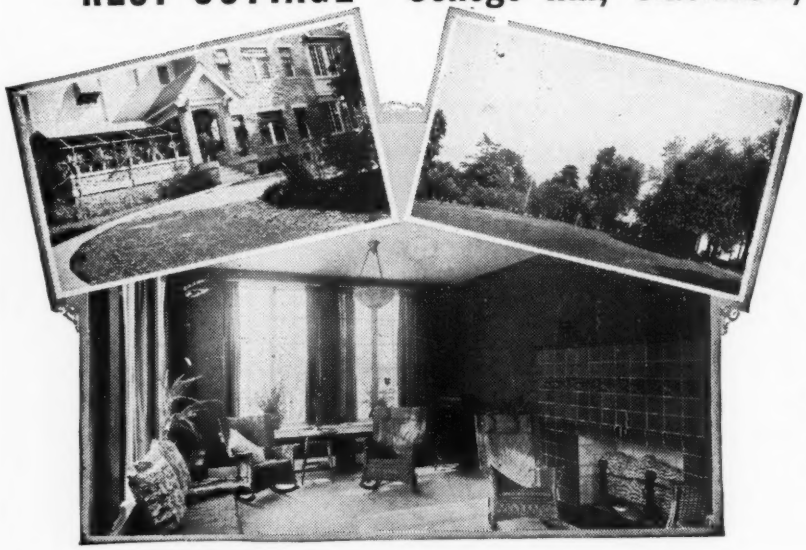

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THE SIGNIFICANCE OF CALCIFICATIONS WITHIN THE LUNGS*

By D. A. RHINEHART, M.D., F.A.C.R.
Little Rock, Arkansas

A large percentage of all roentgenograms of the lungs of adult persons living in urban communities and nearly as large a percentage of those of persons living in rural communities show calcifications within the thorax.[1 2] These vary in amount from those found in a few scattered nodules and nodes to those seen in a widespread dissemination throughout the lungs. Occasionally the amount and distribution is so considerable that a surprising roentgenographic appearance is presented.

Calcification as a pathological process occurs only after necrosis and death of tissue followed by encapsulation. Stages in the chemical reaction probably include the formation of acids and fatty acids and calcium soaps and inorganic salts, finally terminating in the formation of calcium carbonate and sulphate. While elsewhere in the body this process may produce vascular plaques, phleboliths, pleural calcifications, calcified hematomata, and so on, in the lungs, the calcification is always in healed, healing, or encapsulated tuberculous processes.[3]

In some of the pioneer work on tuberculous infection Opie[4] considered as tuberculous in origin all encapsulated and calcified nodules in the lungs, all areas in which calcium had been deposited in caseous material, and all calcified nodes in the hiluses of the lungs and in the mediastinum. Later he[5] wrote that phleboliths, broncholiths, and other forms of calcification form an insignificant proportion of calcified lesions of the lungs. In at least one report[6] on broncholiths that had been coughed up, the roentgen appearance of some of them was typically that of tuberculous calcifications. A study of calcification within the thorax is in reality, then, a study of involvement and healing in different forms of tuberculous infection.

The most commonly encountered kind of calcified tuberculosis is that due to the first, initial or primary, infection with tubercle bacilli, also called by Opie focal infection; and, although it does not always appear in children, it is commonly called "childhood tuberculosis." This usually consists of a calcified focus in the parenchyma and of calcification in the lymph nodes of the hilus of the same lobe of the lung. The nodule in the lung parenchyma usually is sharply defined, circular, oblong, oval, or stellate in outline, with smooth or irregular margins. It may be situated in any part of either lung, not found more often in the apex than elsewhere, and with a tendency to occupy the midportion of the lung. The calcification in the hilus nodes may be in the form of one or more small nodules or in smaller or larger calcified masses (*Fig. 1*).

These evidences of primary infection in tuberculosis are the results of a prolonged process of infection and repair extending over months and even years. The infection usually begins as tubercle formation with collateral infection around the primary focus, or as tuberculous pneumonia or tuberculous bronchopneumonia of greater or less extent found in any part of either lung. The infection extends to those hilus nodes receiving lymph from the involved portion of the lung, producing swelling and caseation. After a time the lesions both in the lungs and the lymph nodes undergo partial resolution and absorption. Sooner or later encapsulation, fibrosis, and calcification appear and they assume their final form.[7 8 9]

The calcified foci of primary infection in tuberculosis are not always single nor are they always small. Sometimes there are two or more calcified nodes in the lungs with corresponding lymph node calcification; less commonly there are multiple lesions. Allison and Medelman[8] be-

*Chairman's Address, Section on Radiology, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

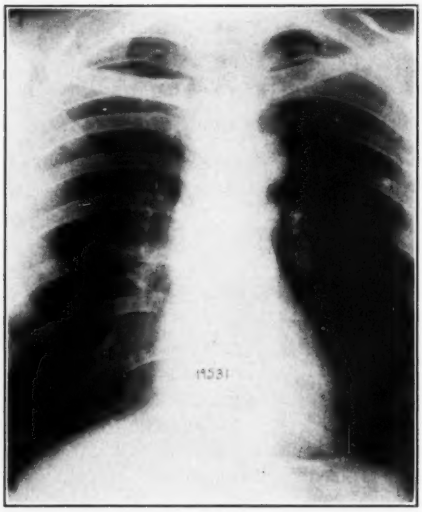

Fig. 1
A calcified nodule in the left lung and calcified nodes in the left hilus region from a primary infection with tuberculosis.

lieve that these multiple lesions are due to caseation and cavitation in the primary tubercles with dissemination of the tubercle bacilli. Opie thinks that they are caused by healed tuberculous bronchopneumonia. They may vary in number from a few widely scattered calcified nodules to a large number involving all portions of the lungs. Opie[5] reported that in one person out of ten these calcified lesions in adults are as extensive as fatal disseminated tuberculosis in children. Multiple lesions vary from those a few millimeters in size to calcified nodules a centimeter or more in diameter. The calcification in the hilus nodes is roughly proportional to the lesions in the lungs, the more numerous and larger the primary foci the more plentiful and larger the calcified lymph nodes.

Opie and Andersen[10] gave a scale for measuring the amount of healed primary tuberculosis in the lungs. Based on the pathological and roentgenological examinations of lungs removed at autopsy, they divided the findings into four groups. In the first group were placed the small nodules in the lungs and hiluses. In the second were those with nodules as much as one centimeter in diameter, with larger masses in the hiluses as much as two centimeters across. In the third group were those showing scattered nodules in the lung substance, with large masses at the hiluses, at the bifurcation of the trachea, or at the side of the trachea above the right bronchus. These masses may reach a diameter of three centimeters. In the fourth group were placed those in which the lungs were thickly and uniformly studded with nodules associated with extensive lesions in the hiluses and around the trachea. Later[5] this grouping was simplified, apparently by combining the third and fourth groups of the first classification.

All of these calcified nodules and nodes are thought to be the result of the first, or primary, infection in tuberculosis, those showing multiple areas of calcification indicating a widely scattered involvement of the lungs from which the individuals had recovered.

From numerous experiences roentgenologists have become familiar with the appearances of the more common forms of calcified primary-infection tuberculosis. Occasionally a film may be seen in which the calcification is in such large amounts that its significance may be doubtful.

Such a film is shown in *Fig. 3.* The patient was a colored boy, 8 years of age. This child did not thrive during his first year, but since then his development has been normal and his health good. A history of an acute febrile illness could not be obtained. When first seen his complaint was of an enlargement of the submandibular lymph nodes. This did not appear to be a tuberculous infection, for it followed an attack of acute tonsillitis and responded to one x-ray treatment. In addition to the large calcified masses in the hiluses, his chest film shows over one hundred fifty separate and distinct

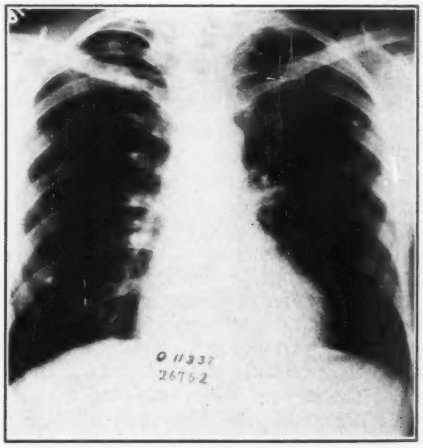

Fig. 2
Calcified nodules and nodes in both lungs and both hilus regions from primary infection with tuberculosis.

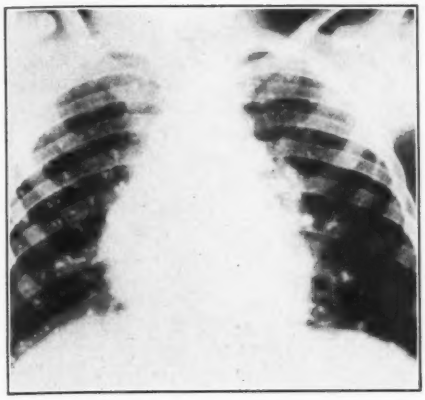

Fig. 3

Multiple calcified nodules in the lungs and large calcified masses in the hiluses in a colored boy 8 years of age due to a primary infection with tuberculosis. In all probabilities this primary infection was in the form of a tuberculous bronchopneumonia.

calcified nodules in the lungs. It has not been possible to arrange for examinations of the other members of this boy's family in an effort to determine a possible contact source for this infection.

Sayers and Meriwether[11] and Sutherland[12] reported instances of multiple calcified lesions in the lungs for which the etiology was obscure. Sayers and Meriwether suggested the possibility that these lesions might be due to a fungus infection; Sutherland that they might result from some undefined anomaly associated with oversaturation of the blood with calcium from drinking water with a high calcium content.

Calcification in the lungs also is found in connection with healing or healed infections of the reinfection or adult type of tuberculosis. Because these infections are relatively not so common as primary infection, and because when they do progress to complete healing, fibrosis is the rule, calcification is not so prominent a feature of this kind of disease.

In his autopsy material Opie[4 5 13] found numerous instances of calcified tuberculous foci in the apices of the lungs of adults dying of other causes which he considered remnants of adult infection. In one out of every five these lesions were present, in addition to those from the primary or childhood infection. When large or multiple, such calcified foci are visible on roentgenograms; but they do not constitute a major portion of the calcifications in the lungs found in living individuals.

If roentgenograms of the lungs of patients with chronic ulcerative tuberculosis are examined for calcifications, those of the primary or focal infection type may be conspicuous, while calcified areas within or adjacent to the regions of active infection are seldom seen. On the contrary, fibrosis is a conspicuous part of the pathological process. This suggests that calcification is not a prominent factor in the healing of such infections.

Occasionally in roentgenograms of living individuals one finds a large number of calcified masses in one or both pulmonary apices. As a rule these are larger, more irregular, and more angular than those of the primary-infection type. Many of them are elongated, with a tendency to be arranged in line with the pulmonary markings radiating upward and outward from the hiluses. Sometimes they are associated with considerable fibrosis extending into the lower zones of the lungs, and there may be exudation, cavitation, and other signs of active infection.

When these calcifications are not associated with the usual signs of chronic ulcerative tuberculosis, they are thought to be the results of an hematogenous type of tuberculosis, a type in which the secondary infection is spread by way of the blood stream of the pulmonary circulation. This is particularly true when the signs of infection and the calcifications are bilateral and symmetrical. Pinner[14] even believes that "calcification occurs only in foci of hematogenous origin." He further says that in the examination of thousands of roentgen series of adults, calcification was not seen unless the lesions suggested the hematogenous type.

Both Pinner[14] and Miller[15 16] describe hematogenous pulmonary tuberculosis. Miller divides the lesions into five types. Two of these are designated as tuberculosis fibrosa densa and tuberculosis fibrosa diffusa, descriptive terms used by French and German investigators. As seen on roentgenograms the x-ray lesions are sharply defined, localized, fibrotic, and calcareous densities of variable extent in the upper lobes of both lungs that are thought to be the healed residues of previous hematogenous dissemination (*Fig. 4*). The only difference in the two forms is that the lesions in one are more extensive than they are in the other.

Miller says that these patients have few or no pulmonary symptoms. They may be poorly nourished and nervous, have digestive disturbances and small repeated pulmonary hemorrhages, but have no cough or fever. Pinner says that the symptoms are variable, some pa-

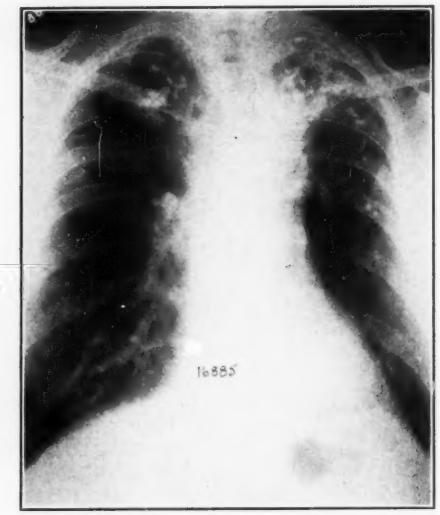

Fig. 4
Multiple irregular calcified lesions in the apices of both lungs from an hematogenous infection with tuberculosis. These lesions did not change in appearance for a period of two years.

tients passing through the infection without being sick. Cough and expectoration are not pronounced symptoms, the physical signs of infection are few or absent, and even on repeated careful sputum examinations only an occasional specimen is found to be positive. Other patients may have the usual symptoms of pulmonary tuberculosis. Miller thinks that care should be taken to recognize this type of infection, for the patients do not require the same treatment as those afflicted with bronchogenic tuberculosis.

Patients having these calcified and fibrotic areas in the apices of the lungs, who also show exudation and cavitation accompanied by cough, expectoration, fever, and the other usual symptoms of tuberculosis, are thought to have a bronchogenic type of tuberculosis grafted onto or following the hematogenous type, probably as a result of ulceration and discharge of a caseous lesion into a bronchus.

Sweany[3] has reported on the autopsy findings of a number of instances of multiple tuberculous calcifications in the lungs. He identified those caused by the primary infection and those due to the hematogenous form. He believes that any tuberculous infiltration that does not excavate into a cavity, but caseates and becomes encapsulated, will become calcified if the time is sufficiently long. He thinks, however, that the calcifications most frequently seen are those of the usual bronchogenic type of tuberculosis occurring in minimal and moderately advanced lesions of long standing, and occasionally in healed advanced disease. He places the hematogenous type next in importance, recognizing a chronic and a benign infection due to this kind of dissemination.

Another and perhaps more interesting type of apparently healed, calcified tuberculosis has characteristics differing from all the others. It is characterized by the presence of a large number of small calcified deposits in the lungs. The lesions are sharply defined and shot-like in appearance. They may be uniformly distributed throughout the lungs or they may be more numerous or localized in the upper lobes. Persons so afflicted may or may not have had an acute illness with recognition of the infection. More often the calcified lesions have been found during routine examinations in persons not giving symptoms of lung infection nor a history of an illness with lung involvement.

This condition seems to have been variously designated. Sante,[17] Blaine,[18] and others have called it healed miliary tuberculosis. Miller has called it tuberculosis miliaris discreta, a term used by French and German writers to designate a relatively mild variety of hematogenous tuberculosis. Pinner speaks of it as a type of hematogenous tuberculosis, and Sweany reported it as a primary-infection type with hematogenous dissemination.

It is quite likely that all these conditions are closely akin to miliary tuberculosis, also a disease with hematogenous dissemination, but one that is commonly thought of as severe and rapidly fatal. Because of the differences in dissemination, virulence of organisms, multiplicity of foci, resistance of the hosts, and so on, there may be numerous intermediate gradations between a rapidly fatal acute miliary tuberculosis at one extreme and a similar infection with few symptoms, recovery, and calcification at the other.

Evidence has been found in support of this idea. Blaine reported three instances of apparently healed miliary tuberculosis of the lungs. Opie[19] was of the opinion that miliary tuberculosis may heal. Sante reported evidence indicative of a chronic form of miliary tuberculosis and showed roentgenograms of patients with healed miliary tuberculosis. Many other similar reports, some showing observations of the patients from the acute stages to recovery, have been found, but to save repetition they will not be cited. Roentgenograms published by Sweany, Pinner and Miller, as evidences of healed hema-

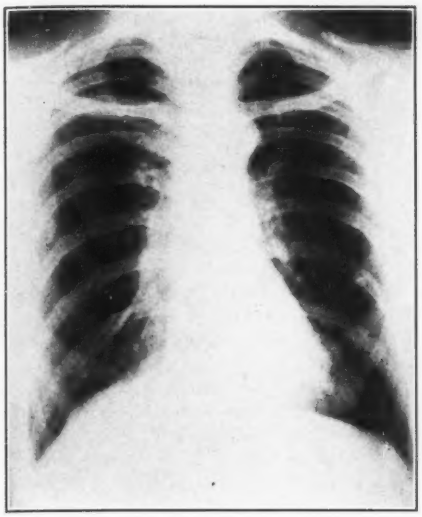

Fig. 5

A large number of minute shot-like calcifications uniformly scattered throughout both lungs thought to be the results of a healed miliary tuberculosis.

togenous tuberculosis and called by Miller tuberculosis miliaris discreta, are identical with those of Blaine and Sante illustrating healed miliary tuberculosis. The differences then may appear to be only in the terminology used in designating the kind of infection present.

Two cases, one of which presents several unusual features, will be briefly reported illustrating this kind of hematogenous pulmonary tuberculosis.

The first is that of a white girl who was 7 years old. Four or five months before this patient was first seen she developed an adenitis of the occipital, submandibular, and upper deep cervical lymph nodes. She was taken to a physician, who removed her tonsils. This made her general condition worse and she rapidly lost weight. While she had a continuous fever, her temperature never was high. On admission to the hospital she showed the adenopathy and some emaciation. The physical examination was essentially negative. A roentgenogram (*Fig. 6*) showed a widely disseminated pulmonary tuberculosis. A calcified focus of primary infection is not apparent on this film. I am still uncertain whether or not any of the lung lesions show calcification. Tubercle bacilli were found in a smear from the throat. The patient died two weeks after this examination was made.

The second patient has been under observation since June, 1927. At that time she was a young white woman, 18 years of age, who had been married for six months and who was about three months' pregnant. Her complaint was shortness of breath of a month's duration, some nausea and vomiting, and high fever. Two weeks before she had had a tooth extracted, the fever starting a week later.

On first examination a respiratory rate of 30 to 50 each minute and a temperature as high as 104.6° F. were the chief findings. The breath sounds were increased over both lungs and fine crepitant rales could be heard throughout the lungs. A roentgenogram of the chest (*Fig. 7*) showed what was thought to be a widely disseminated pulmonary tuberculosis. The lesions all appeared to be soft with poorly defined margins. She remained in the hospital for thirty days. She improved slowly and gradually. The temperature gradually declined, and the respiratory rate lessened. A

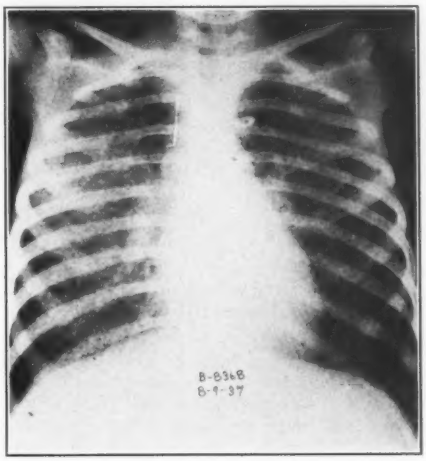

Fig. 6

Widely disseminated tuberculous lesions in a white child 7 years of age. A fatal type of disseminated tuberculosis.

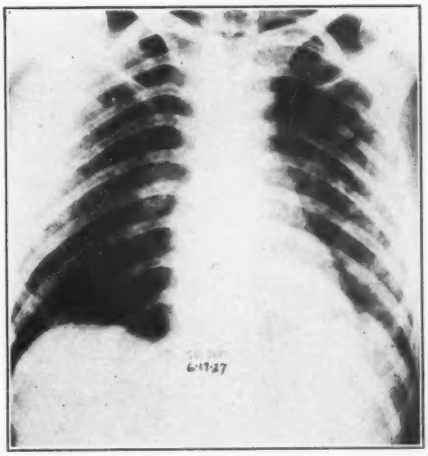

Fig. 7

Widely disseminated pulmonary tuberculous lesions in a white female 18 years of age. This film was taken during the acute stage.

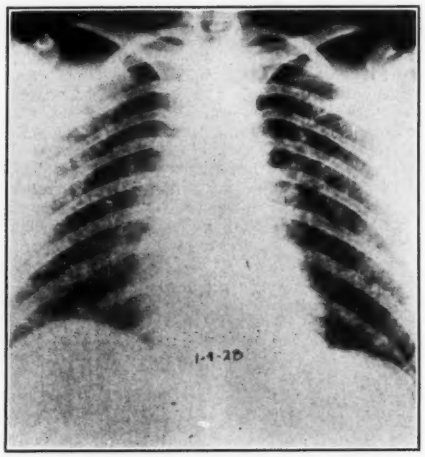

Fig. 8

A film of the chest of the same patient shown in Fig. 7 taken six months later showing a decrease in the size and beginning calcification of the lesions.

second roentgenogram made at the end of the hospital period showed some decrease in the size of the individual lesions and some increase in their density.

The patient continued under her physician's care after she left the hospital. She remained continuously in bed. The fever continued with daily elevations of temperature to 100° F. or more. Six months after the first admission she returned to the hospital for a cesarean operation. Her recovery from this was rapid and uneventful. Before she left the hospital a third roentgenogram was made (*Fig. 8*). This showed further decrease in the size and an increase in the density of the lesions in the lungs.

Following this operation the patient was again kept in bed for another six-month period. She slowly improved, finally became fever-free, and was permitted to be out of bed. In April, 1928 she was operated upon for acute appendicitis. In 1930 a roentgenographic examination of the lungs showed what was thought to be a complete calcification of the lesions in the lungs. On April 8, 1937 she had a second cesarean operation. The latest roentgenogram (*Fig. 9*) was made in October of this year, more than ten years after the first examination.

This patient now has few complaints. The chief of these is dyspnea on exertion, which easily can be attributed to the decrease in lung volume from the calcifications. On five or six occasions she has coughed up small hard concretions, but there have been no hemorrhages. The two operations and a roentgen examination did not show any calcifications within the abdomen. Both children are living and well, the older one showing typical calcified lesions of primary tuberculous infection.

This patient has had what seemed to be a disseminated form of hematogenous tuberculosis with innumerable separate and distinct foci within the lungs. She was under observation through most of the acute stage, during the slow convalescence, and for a sufficient period of time for the foci apparently to calcify completely. She is an illustration of the fact that the infected areas in even the most widely disseminated pulmonary tuberculosis of the hematogenous form may ultimately heal and calcify.

In some instances pulmonary calcifications may be clinically important. Children showing positive tuberculin reactions and calcified primary lesions in the lungs do not seem to be benefited by sanatorium or special school therapy. It seems to be much more important to protect them from contact with an open case of tuberculosis during puberty and early adult life, and to examine them periodically in order to detect an adult reinfection or secondary type of infection at the earliest possible time. Some calcified pulmonary masses have caseous centers in which are living tubercle bacilli. Through disintegration or rupture these bacilli may be liberated into the bronchial tree or the blood or lymph vessels and be the source of an endogenous tuberculosis. Probably the widespread acute tuberculous infections occasionally seen in adults originate in this manner.

SUMMARY

Calcification in the parenchyma of the lungs and in the lymph nodules and nodes within and in connection with the lungs is always tubercu-

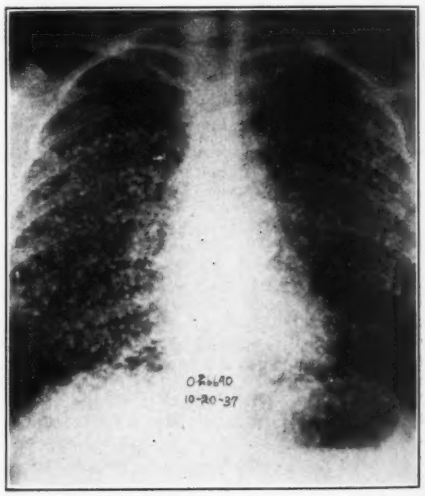

Fig. 9

A film of the chest of the patient shown in Figs. 7 and 8 taken ten years after the acute illness showing complete calcification of the lesions.

lous in origin. The most commonly seen type is that occurring as a result of the primary infection with tuberculosis, usually called childhood-type tuberculosis. This may be present as a single nodule in the lung with involvement of the lymph nodes; as nodules and nodes in more than one lobe or in both lungs; and as multiple calcified nodules, probably from a tuberculous bronchopneumonia, scattered throughout the lungs, and associated with large calcified lymph node masses. Calcification may occur in the healing of tuberculosis of the bronchogenic form. In hematogenous pulmonary tuberculosis calcification may be found in considerable amount, usually symmetrically distributed, and most often in the upper lobes of the lungs. Large numbers of small calcified nodules distributed throughout both lungs indicate a healed disseminated tuberculosis of the hematogenous type. An infection of this kind may be a form of miliary tuberculosis of the lungs that progresses to recovery and complete calcification of the lesions.

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ARTIFICIAL FEVER THERAPY IN SKIN DISORDERS*

CLINICAL AND BIOCHEMICAL STUDIES WITH SPECIAL REFERENCE TO THE PHYSIOLOGY INVOLVED

By A. Buist Litterer, B.S., M.D.
and
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The rapidity with which artificially produced fever has invaded the field of therapeutics is little less than astounding. The clinical application of artificial temperature in dermatology is apparently assuming its definite place in this development. Recent and current investigations reveal a trend on the part of clinical research workers to broaden this application in skin disorders. In reviewing the literature briefly, we find that the therapeutic value of fever was recognized as early as the Eighteenth Century according to Tillmans.[1] Ricord and Dupres noticed its favorable influence on syphilis. Bazin,[2] in 1862, McVail,[3] in 1898, and MacLeod,[4] in 1900, report favorable results in mycosis fungoides after an attack of erysipelas. Tulipan and Director[5] report encouraging results in patients with generalized dermatoses treated with typhoid vaccine intravenously. In their series of 12 cases, 3 showed complete resolution, six improvement, and there was no effect in three. Since the introduction of artificial fever therapy by electrical means, many workers have reported successful results in diseases such as chorea, paresis, gonorrhea and chronic asthma, but little is known of its therapeutic value in cutaneous diseases. Bierman[6] reports temporary results in scleroderma, mycosis fungoides and Kaposi's sarcoma. Feinberg, Osborne and Steinberg report excellent results in a case of chronic eczema and chronic urticaria associated with asthma. Klauder[8] reports a case of mycosis fungoides which showed progressive improvement. Rosen, Rosenfeld and Krasnow[9] report temporary clinical improvement in seventeen of eighteen patients with generalized chronic recurrent dermatoses. Of this series four remained well for a period of four months, four showed mild relapses after a few weeks and three had severe relapses. The other cases passed from observation.

While most of the completed reports primarily circumscribe a group of cutaneous lesions usually termed "resistant, recurrent or allergic derma-

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toses," they also open new avenues of speculation into the whole field of metabolism as related to general skin disorders.

It is the aim of this report briefly to discuss the clinical application of artificial fever, produced by physical means, to certain skin disorders and further to elaborate upon the possible underlying changes in metabolism responsible for the responses obtained. Establishment of proper technic, together with preferable choice of apparatus, are also important factors in the problem.

One hundred and sixty-seven patients with cutaneous diseases have been treated by fever therapy over a period of the past four years. The total group segregates itself into the following classifications: eczematoid group with or without other allergic manifestations, fifty cases; multiforme erythema, ten cases; psoriasis (acute and chronic), six cases; endocrinopathies with cutaneous manifestations, fifteen cases; urticaria, eighty cases; seborrheic dermatitis, six cases. The variations in age, sex, duration of the disease, together with the technic, observation periods and clinical results, are summarized in *Table 1.*

Careful study of the table reveals many points of interest and value. The importance of a sufficient observation period, together with proper evaluation and close study of the relapse ratio, is self-evident. Unless these two factors are observed closely it is clearly seen that the clinical results will be totally misleading.

It will be found that in the eczematoid group a 96 per cent immediate response is obtained and this high ratio of improvement continued well into the fourth month of observation. Between this and the fourth year, however, we note a relapse of 31¼ per cent of those who received a complete clinical remission of their cutaneous lesions immediately following the course of fever treatments. The lack of proper evaluation of this important observation, relapse ratio, has undoubtedly been responsible for many clinical reports, including those by allergists, which failed to be confirmed by other investigators.

The multiforme erythema cases were all chronic and had proven themselves resistant to all forms of previous treatment. The immediate response revealed a complete resolution in 90 per cent, which again extended well into the fifth month. But, as above stated, by continuing close observation over a period of two years, we find a relapse ratio of 33 1/3 per cent. Psoriasis revealed a 50 per cent immediate response, but within four years 33 1/3 per cent had relapsed. A case is well worth brief mention in detail.

A young woman of 29 years was first observed four weeks after the onset of acute psoriasis. Fever therapy improved her about 75 per cent. Fearing a possible relapse, six intravenous injections of 0.45 gm. of neoarsphenamine was administered without further improvement in the skin. After the last injection she left the city and within the ensuing four days she became exposed to a sunburn. Within three days she developed the most severe fulminating arsenical dermatitis we have ever observed. By the time she could return to the city, the reaction was so intense that no one expected her to survive. There was marked generalized edema, especially involving the face and legs with a deep purplish flush. Oozing was prominent in the flexures and

Table 1

RESULTS OF FEVER THERAPY BY ELECTROMAGNETIC INDUCTION IN 167 CASES SUFFERING FROM CUTANEOUS DISORDERS

Disease	Total Cases	Sex	Ages	Duration	Temperature	Number Treatments	Observation	Immediate Response	Relapse
Eczematoid	50	M.—30 F.—20	3-52 yrs	6 mos.-20 yrs	103-105° F.	6-20	3 mos.-4 yrs	48-96 per cent	15-31¼ per cent
Multiforme erythema	10	M.— 8 F.— 2	29-45 yrs	3-10 yrs	102-104° F.	6-10	6 mos.-2 yrs	9-90 per cent	3-33 1/3 per cent
Psoriasis	6	M.— 2 F.— 4	23-38 yrs	1 mo.-4 yrs	101-103° F.	6	6 mos.-4 yrs	3-50 per cent	1-33 1/3 per cent
Endocrine	15	M.— 5 F.—10	10-18 yrs	1- 5 yrs	102-104° F.	6-18	4 yrs	12-80 per cent	0- 0
Urticaria	80	M.—30 F.—50	14-39 yrs	2 wks-5 yrs	102-106° F.	6-18	3 mos.-4 yrs	50-62½ per cent	30-60 per cent
Seborrheic dermatitis	6	M.— 3 F.— 3	12-32 yrs	15 mos.-1 yr	102-104° F.	6-10	1 yr	6-100 per cent	1-16 2/3 per cent

dependent portions of the body. Complete desquamation resulted over every inch of her body, including the scalp and nails. She was confined to the hospital for four months, during which time she suffered extreme toxicosis and prolonged high fever with the exception of the last two weeks. However, eventually she made a complete recovery. After this attack of arsenical dermatitis, complete resolution of the psoriasis was evident and at this time (four years later), she has a most perfect skin of velvet-like texture. There has not occurred during this period even as much as a single patch which would indicate any sign of recurrence of her psoriasis. The prolonged fever in this case was of probable significance.

The endocrine group needs some further elucidation. This represents a class of patients who presented various and sundry cutaneous manifestations, some eczematoid in character, some pseudo-urticarial in nature, and others a modified myxedema with dry, scaly, non-functioning skins, the integument especially of the legs, presenting a modified ichthyosis. They presented an associated polyglandular imbalance, which had sedentery habits, low metabolism, blood pressure, poor digestion and elimination. They usually fell in the younger or low middle age group. The immediate response to fever therapy with complete abeyance of their cutaneous manifestations was 80 per cent. After four years' observation, there have been no relapses, due apparently to the proper functioning of the endocrines after they were given a boost by raising the general metabolism.

Study of the table reveals a very important consideration in urticaria. It will be noted that only a 62½ per cent immediate response was obtained and 60 per cent of these relapsed. In addition to these eighty cases, a group of seventy-five cases has been studied over the past seven years with reference to the part played in the etiology by underlying systemic conditions. In over 90 per cent there can be demonstrated by thorough study abnormal upsets in one or more of the gastro-intestinal, liver and biliary, or endocrine systems. When these conditions are isolated and the treatment consists of correcting them in addition to fever therapy, the immediate response immediately rises to 85 per cent and the relapse ratio drops to 25 per cent. So successful has this combined management been in our hands that we have practically discontinued skin testing and attempted desensitization in urticaria.

Physiological Discussion.—From a critical analysis of the clinical portion of this study it must be admitted that the results are decidedly encouraging and justify further investigation. The treatment of these cutaneous disorders has been notoriously discouraging. Reference to a report by Rosen, Rosenfeld, and Krasnow,[9] together with their bibliography, will adequately confirm both of these statements.

Much light is thrown upon the mechanism of both the etiology and response of these cutaneous disorders by a study of physiological and biochemical changes already established during fever therapy. There remains little question that the two great regulators of body temperature balance in the normal, are the heat regulating mechanism in the brain base and the proper function of the skin. Recent physiological investigations[10 11] have just as definitely established that temperature changes at the brain base center invoke an immediate reflex response in the circulation at the surface with an associated fluctuation in the elimination of water and crystalloids through the excretory ducts. A study of *Figure 1* is helpful in that it revives a much forgotten clinical picture. The picture reminds us again of the character of the corkscrew coiled nature of the excretory ducts, the function of which is to cause delay in excretion in order for proper separation between colloids and crystalloids to take place. We are further reminded of the existence of the great subcutaneous lymph space in which a great portion of the

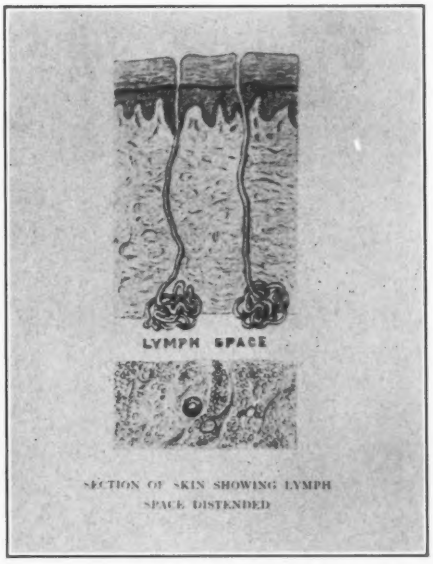


Fig. 1
Sagittal section of skin showing great lymph space, coiled ducts and their communication to surface.

total body chemical changes are carried on. There are many underlying circumstances which can result in overproduction of irritating or toxic bodies at the periphery whereby this expansile lymph space becomes distended and surcharged with such products. Spasm of the smaller vessels, as well as the delicate ducts, and to some extent of the smooth masculature with vascular stasis, can all be assumed in logical sequence. This further decreasing elimination set up a vicious cycle with the resulting distention edema and passive congestion with the final thickening, characteristic of many of these disorders. The same essential end result in the great subcutaneous lymph space may come about through a mechanism from without in. Underlying circumstances which produce peripheral changes in the skin surface structures resulting in scaliness, thickness, or overproduction of sebaceous material plugging the excretory channels will produce a back-up into the underlying lymph space.

That fever therapy exerts its benefit by strik-

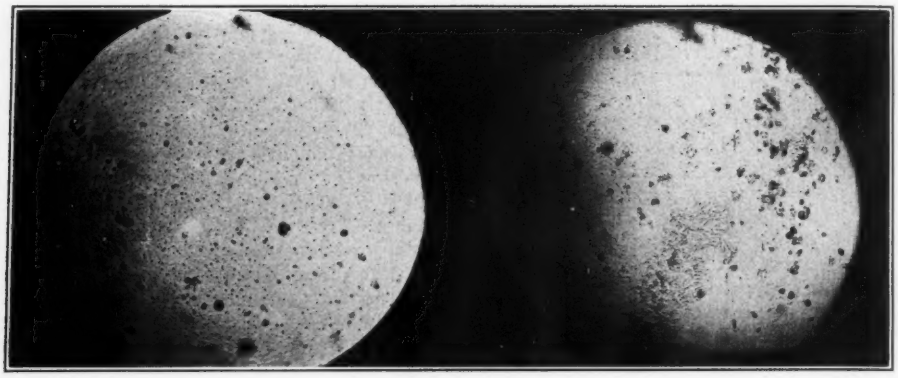


Fig. 2-a Fig. 2-b

Generalized Eczema

2-a. Crystals isolated from sweat following eight hours' rest showing large circumscribed dots of calcium lactophosphate.

2-b. Crystals isolated from sweat following eight hours' rest. Note calcium lactophosphate, spicules of lacto-ammonium chloride, daggers and petals of urea and sodium chloride.

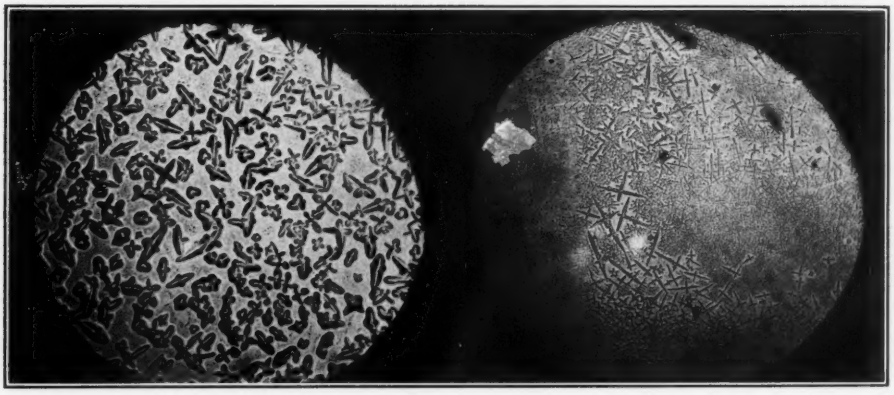


Fig. 3-a Fig. 3-b

Generalized Eczema

3-a. Crystals from sweat following fever of 105° F. by penetrating heat. Abundance of dagger and flower petal crystals represent urea and sodium chloride in different combinations. Calcium lactophosphate dots are interspersed.

3-b. Crystals from sweat at 105° F. (penetrating heat). Typical daggers of urea and sodium chloride with the chloride in excess; spicule type are lacto-ammonium chloride; calcium lactophosphate interspersed.

ing at this very mechanism is indicated by physiological and biochemical study. It was first established by Barbour[11] that when heat was applied to the temperature regulating center there resulted a peripheral vasodilation, increased perspiration and skin elimination with an increase in general heat loss. Rosen, Rosenfeld, and Krasnow have studied the biochemistry of the blood with respect to cholesterol, albumins, globulins, lecithim and lactic acid, and of the sweat in many of these resistant dermatoses. They found a decrease in free cholesterol ranging from 26 to 49 per cent in 81 per cent of the cases. The other elements did not show a definite trend. In the sweat, however, increase in lactic acid excretion during fever therapy was noted, as well as changes in the pH.

Preliminary studies on the sweat were reported by Phillips and Shikany[12] in connection with fever therapy in 1935. In this study changes in urea, lactic acid, sodium chloride, calcium and sugar were all indicated, but they could not be obtained quantitatively. We have since been able to progress in this study by utilizing the study of specific crystal formation as a means of identifying substances. This method of study simulates a similar study in 1893 of the sweat

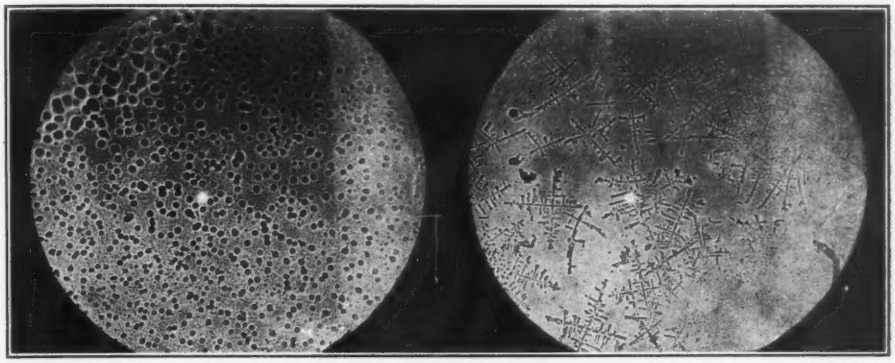


Fig. 4-a Fig. 4-b

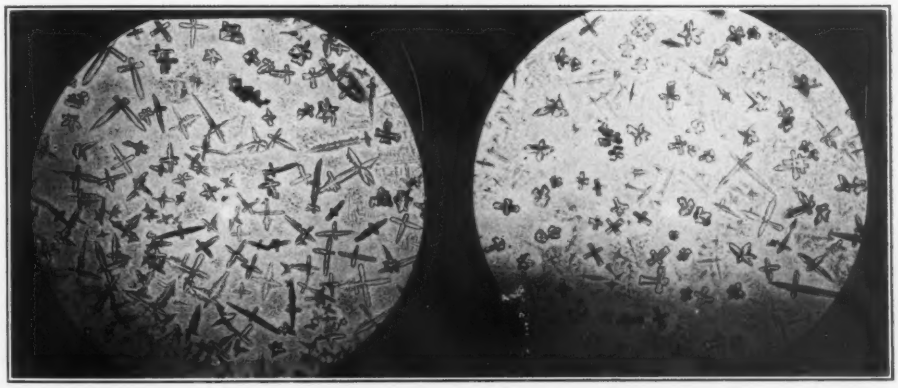


Fig. 4-c Fig. 4-d

Crystals made by synthesis for purpose of identification.

4-a. Lactic acid plus calcium phosphate. Specific large sharply circumscribed dots of calcium lactophosphate.

4-b. Lactic acid plus ammonium chloride. Long bars with spicules attached at right angles. These crystals are very unstable. Note that they undergo change within a few moments after preparation.

4-c. Sodium chloride plus urea (NaCl in excess). In this combination the large dagger crystals predominate in the field. Note occasional spicule type of lacto-ammonium chloride undergoing transformation into urea.

4-d. Sodium chloride plus urea (urea in excess). In this combination the flower petal crystal predominates.

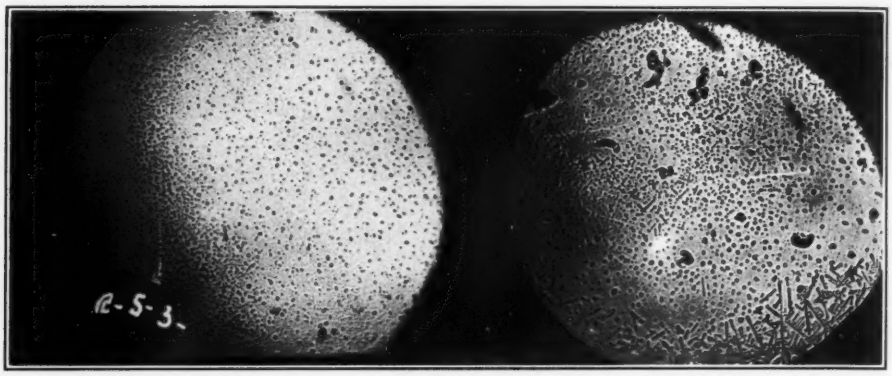


Fig. 5-a Fig. 5-b

Generalized Eczema

5-a. Crystals from sweat during fever by external heat (dry bulb cabinet). Excretion chiefly calcium lactophosphate.

5-b. Crystals from sweat following fever by external heat (electric blanket). Calcium lactophosphate predominating; lacto-ammonium chloride and occasional sodium urate. Note the tremendous decrease in amount of excretion products as compared to Fig. 3 (a) and (b) by penetrating heat.

in rheumatism by Percy Wilde[13] of Bath, England.

Figure 2 represents crystals from evaporation of sweat collected eight hours following rest, in a case suffering with a severe, extensive eczematoid eruption. The cutaneous manifestations extended quite generally over the face, neck, upper portions of chest, arms, hands, legs and dorsum of the feet. The skin was much thickened and edematous with a dusky tinge over the extremities from vascular stasis, with some weeping and evidence of excoriations from the intense pruritis. The predominant crystals are those of calcium, lactophosphate with traces of lacto-ammonium chloride characterized by spicules, and combinations of urea and sodium chloride which form the flower petals and dagger type of crystals.

This patient was now exposed to fever therapy, raising the body temperature to 105° F. by electromagnetic induction combined with an air conditioned cabinet which was maintained at a temperature of 105 to 110° F. and a humidity of 85 to 90 per cent saturation. Sweat collected during the treatment reveals an extensive excretion of urea in combination with sodium chloride, lacto-ammonium chloride, with some calcium lactophosphate (see *Fig. 3, a* and *b*).

These substances are identified by their specific crystals which have been prepared by synthesis as shown in *Fig. 4* (*a, b, c* and *d*). There can be little question that the subcutaneous lymph space in this condition was surcharged with lactic acid and nitrogenous end products and that ammonia, calcium and sodium chloride all have a definite function in caring for this condition. They are then excreted through the skin ducts in various combinations. Interestingly enough, the blood urea, calcium chlorides, and lactic acid, showed no significant changes from normal. The blood was, of course, drawn at the same time that the sweat was collected. This would indicate that the biochemical changes involved were taking place in the great subcutaneous lymph spaces, and that the excretory prod-

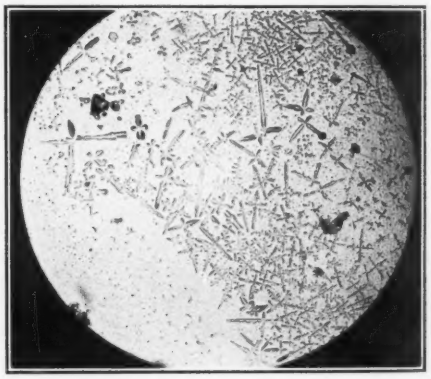


Fig. 6

Erythema Multiforme

Crystals from sweat during fever by electromagnetic induction. Urea and sodium chloride, lacto-ammonium chloride and calcium lactophosphate are all shown.

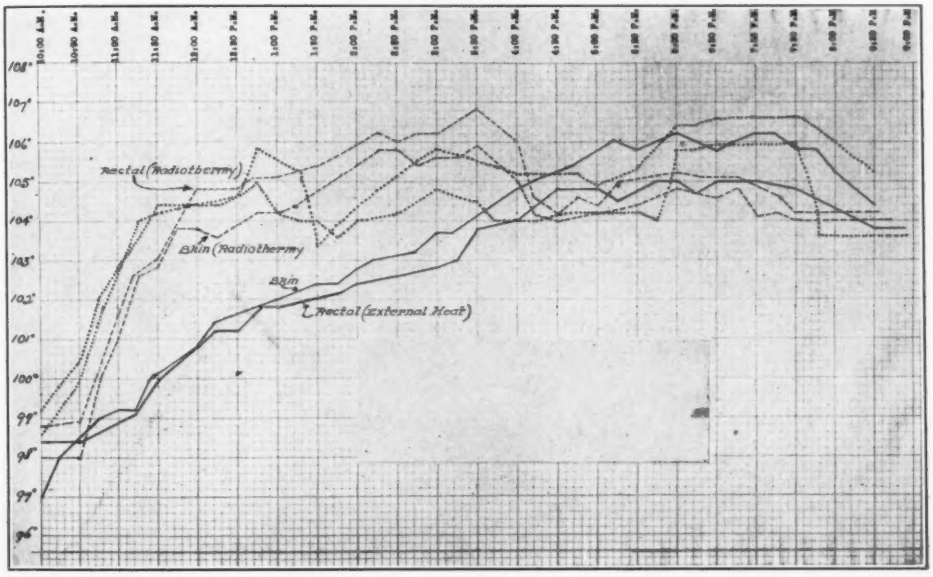
ucts were not from excessive protein tissue breakdown as a result of the fever.

Reference to *Fig. 5* (*a* and *b*) reveals a most significant observation. Under fever produced by external heat to the skin, where the normal gradient between the skin and internal temperature is reversed, we find a marked decrease in the excretion products with the exception of the calcium lactophosphate.

Figure 6 reveals, in the case of erythema multiforme, the same combinations being eliminated through the skin as evidenced by the crystals from the sweat. One is, therefore, much inclined to suggest that there might be a common underlying toxic or metabolic background for many of these resistant dermatoses and that their response to fever therapy comes through the channels of increased metabolism (7 per cent for each degree Fahrenheit of temperature) increased circulation and oxidation, together with increased skin elimination.

For further control information regarding this point, six normal healthy volunteers were exposed by electromagnetic induction and the air conditioned cabinet to fever of 105° F. and their sweat failed to show any such crystals except for occasional calcium lactophosphate, urea and sodium chloride crystals. Blood chemical analysis remained normal.

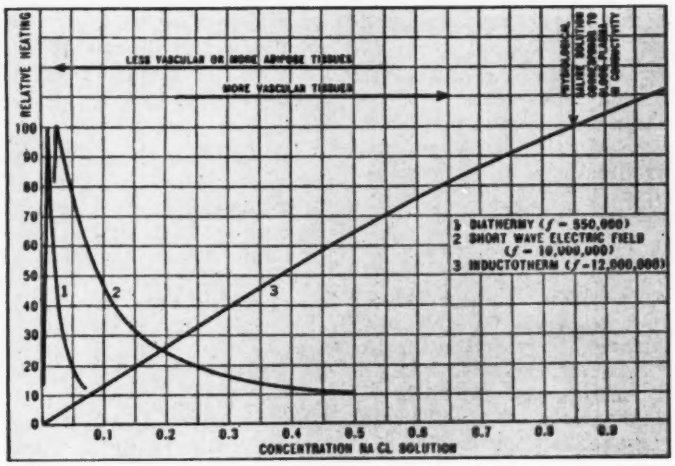
Machines and Equipment—It is obvious from analysis of the above discussion that the choice of apparatus for producing the fever is of vital importance. In the normal there exists a physiological gradient between internal body temperature and skin temperatures. The surface of the skin functions at a much lower temperature than that of the interior. Neymann and Holmquest[14] have shown that when the rectal temperature is 37.2° C. (99° F.) the temperature of the skin registers between 33.8° C. (93° F.) and 35° C. (95° F.). This physiological gradient should be maintained as nearly as possible during fever therapy in order to allow the skin to be free to function and eliminate. Such is the case when the fever is produced by penetrating heat. On the other hand, when the fever is produced by external heat, the skin is baked and in order to produce the rise in internal temperature, this



Graph 1

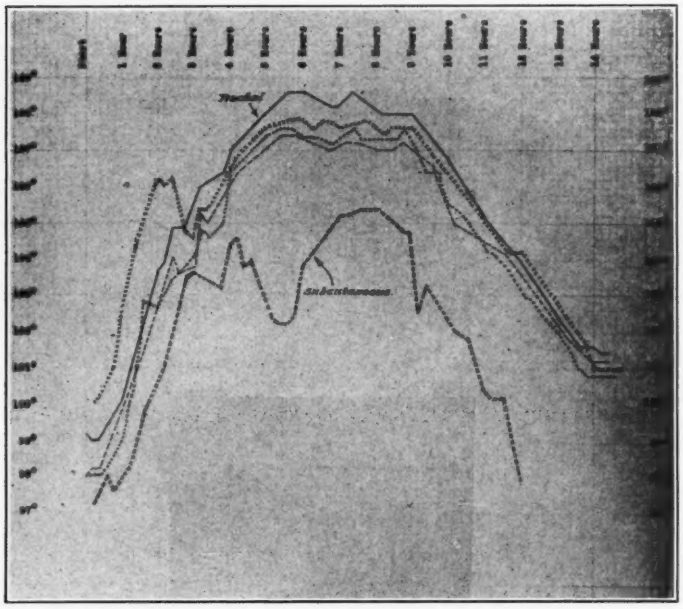
Illustrating the difference between skin and internal temperature during fever produced by penetrating and external heat. Note that during external heat the skin temperature remains constantly higher than the internal temperature, while with penetrating heat it remains lower. (After Neymann and Osborne.)

Key: ———Electric Blanket
- - - -Radiothermy
. . . . . .Diathermy


RELATIVE HEATING
LESS VASCULAR OR MORE ADIPOSE TISSUES
MORE VASCULAR TISSUES
1 DIATHERMY (f = 550,000)
2 SHORT WAVE ELECTRIC FIELD (f = 10,000,000)
3 INDUCTOTHERM (f = 12,000,000)
CONCENTRATION NA CL SOLUTION

Graph 2

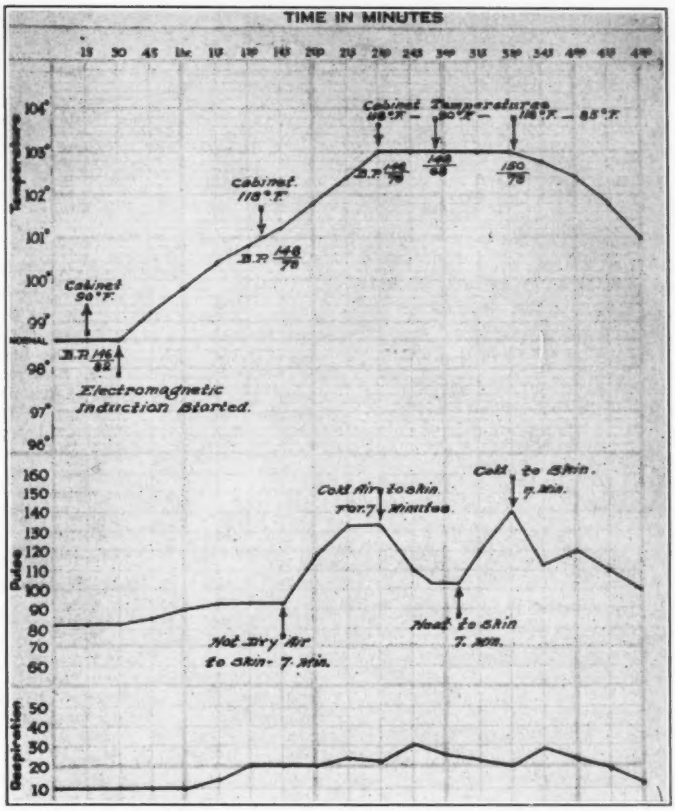
Showing the comparative heating effect upon electrolytes in different concentrations by diathermy, radiothermy and electromagnetic induction. Note that maximum heating by induction occurs at 0.85 per cent (physiological) concentration as compared to 0.1 per cent with the other two (Merriman, J. R.; Holmquest, H. J.; Osborne, S. L.: Amer. Jour. Med. Sci., **187**:5 (May) 1934).



Graph 3

Illustrating the lowered degree of heat produced in the subcutaneous tissue (great lymph space) during fever produced by penetrating heat (diathermy). The skin is cool and free to eliminate while the internal temperatures parallel each other. (After Neymann and Osborne.)

Key: ——————— Rectal temperature
xxxxxxxxxxxx Lumbar spine
. . . . . Cisterna magna
- - - - - - - - - - - Axillary
═ ═ ═ ═ ═ ═ Subcutaneous



Composite average temperature and pulse ratio curves in six normal volunteers under skin stimulation. (After Phillips and Shikany.)

Graph 4

Showing direct relationship between pulse rate and skin temperatures. Note the independence between heart rate and the general body temperature.

physiological gradient must be reversed and the body subjected to a phenomenon similar to a roast in an oven. This important factor is clearly illustrated in *Graphs I* and *III*, which demonstrate a comparison between the external and penetrating heat methods of fever production.

In the application of artificial fever to skin disorders, two additional factors must be given consideration. Although penetrating heat is the method of choice it is still most desirable to escape the use of electrodes or contact points having to be applied directly to a skin already abnormal. Secondly, unless a machine of proper frequency is used, there is danger of arc formations with the pools of perspiration formed, and serious skin burns may result. Both of these handicaps are ideally overcome by using inductothermy in conjunction with the air conditioned cabinet. In this set-up the patient is placed within the electromagnetic field free from direct contact and due to the high saturation of moisture (85 to 90 per cent) the cabinet temperature is maintained at 105 to 110° F., a perfectly safe temperature for skin tolerance. Merriman, Holmquest and Osborne[15] have demonstrated (*Graph II*) the explanation for the relative safety in the electromagnetic field by showing that its maximum heating capacity is near physiological concentration of electrolytes while that of radiothermy and diathermy exert their maximum in the lower ranges which would include tissues and sweat.

That important reflex terminals probably exist in the skin and must be considered is indicated by *Graph IV*. Phillips and Shikany[12] have shown the important connection between the temperature of the skin and the heart rate. This in part accounts for the differences reported in pulse rates during fever production by external and penetrating heat.

In skin disorders involving changes which have already decreased the normal skin function, it would seem to be vital that we utilize all means to aid and promote skin elimination. Fever production by the electromagnetic field in combination with the air conditioned cabinet with high humidity and relatively low temperature, would appear to be the method of choice.

CONCLUSIONS

(1) Skin disorders such as are herein described are known to be resistant to conventional treatment.

(2) Distinct clinical value of fever therapy in these disorders is indicated.

(3) Physiologic and biochemical studies indicate that metabolic changes are produced in the subcutaneous lymph space during fever therapy in this group of skin disorders.

(4) Penetrating heat is believed to be superior to external heat in fever production, and electromagnetic induction, together with proper air conditioning, appears to be the method of choice.

(5) A method of studying elimination products through the skin by crystallization of the sweat is demonstrated.

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DISCUSSION (*Abstract*)

Dr. Wm. F. Spiller, Galveston, Tex.—Artificial fever is still a comparatively new field. Our experience with fever therapy in syphilis is past the experimental stage and shows beyond a doubt that fever combats an infectious process. Therefore, it is reasonable that skin disorders, which are due to an infectious process, should be benefited by this treatment. This paper contributes more proof along these lines, and has gone a step further. The authors have obtained results in cases that are not of infectious origin.

The results obtained by them in urticaria and the endocrine disorders are encouraging indeed, and there were no relapses in the endocrine cases. This alone is a long stride forward in dermatological therapy.

Observations are as yet too incomplete to evaluate the therapeutic efficiency of artificial fever, for here we do not get the changes that we get in fever due to systemic intoxication.

Enough cases have been reported to prove that erysipelas and malaria produce a beneficial effect on mycosis fungoides. Here other factors than febrile reaction were concerned, and I feel that we get biologic factors other than the fever.

The excellent demonstrations presented show, beyond a doubt, that metabolic processes do take place in the skin during artificial fever.

It is generally accepted that most of the "resistent, recurrent" skin disorders mentioned in this paper are benefited by fever therapy. It is yet to be determined which type of fever is the best to use and the proper technic and apparatus to employ. I am more familiar with diathermy, but here you have an added element of danger from burns. The machine used by Drs. Litterer and Phillips seems to be excellent. We must consider: does the end result justify the means? Are our results good and are they temporary or permanent?

I recently treated a case of general paresis that had an extensive psoriasis with malaria. The psoriasis cleared up, yet I would hesitate to give malaria for psoriasis. However, if I could produce the same result by physical means, I should feel justified in doing so.

There are economic aspects to be considered: the cost of treatment, loss of time from work, and the fact that fever therapy requires hospitalization.

Dr. Howard King, Nashville, Tenn.—My experience with artificial fever produced by this method and my observation of cases treated by it amounts to exactly nil. I have observed some other forms of artificial fever therapy in some of the diseases just recited and noted rather indifferent results. Whatever comment I make is only that of a dermatological bystander.

When one reviews the subject of artificial fever therapy in its various forms as heretofore used, his first

thought as a practitioner naturally turns to the hazards which accompany it. Many regrettable experiences have been related. In the approach to such a procedure the first consideration is the reduction of all harmful effects to a minimum. The particular method practiced by these gentlemen in this piece of work seems to have accomplished this to a remarkable degree of satisfaction. In closing the discussion I hope they will give us more intimate details about the working of the apparatus.

They are to be admired in their fearless choice of tough dermatological problems, namely: eczema, psoriasis, chronic urticaria and erythema multiforme. These things are not the rare problems which beset us all, but are the common pests which give the dermatologist alopecia prematura.

The percentage of temporary alleviations compare splendidly with all other forms of artificial fever. For that matter, it has been very good by many other methods.

The relapse ratio in this series of cases is the best I have been able to find. It is true, sufficient time has not elapsed to offer claims for permanency of results, but these observations even this far should warrant some speculation as to permanency of outcome, and from that standpoint it is most cheerful. Certainly it shall justify further work along this line, hoping that studies of sweat will reveal more about impaired physiology in these conditions and perhaps finally clarify the whole etiology.

Lastly a very important question arises. Is this particular type of apparatus adaptable to a fairly general hospital use? If so, can it be made to reach the public at large with a relative degree of safety?

Dr. J. Lamar Callaway, Durham, N. C.—For the sake of accuracy I should like to raise an objection to the use of the term "sweat" throughout Drs. Litterer and Phillips' paper. They have collected both sweat and sebaceous material, and though there is perhaps no intrinsic significance in the presence of the sebaceous material as far as their studies are concerned, I feel that the term "sweat" is not an exact description of the material studied.

I am not sure that the controls were completely satisfactory for the material obtained in this group was from sweat glands in the axillae which are predominantly of the apocrine type, while material studied from the patients in the series was for the most part obtained from eccrine sweat glands. These factors may or may not be of any great importance, but their presence should be recognized.

Dr. Phillips (closing).—Dr. King has raised the question of general application and safety. In the hands of those experienced and trained in fever therapy, and with equipment of the latest design, properly located in an institution, we may consider it perfectly safe to administer the temperatures required in the skin conditions. Please, however, allow me to reemphasize that in these conditions the skin must be cool and free to eliminate. This important requirement is defeated when the baking type of apparatus is used, which produces its fever effect by virtue of the same phenomena as a roast in an oven. The surface is browned, so to speak, and the juices are sealed in.

Dr. Callaway offers an interesting objection. I am not personally aware of any studies on the sweat which first separated it from the sebaceous material. It has been my impression that such material would be present in all sweat. Should this impression be incorrect and the term "sweat" under such conditions likewise be not correct, then I suppose we have blundered and should have called it "skin secretion" or some such term.

In cases with a thickened, dry and poorly functioning skin, during mild fever we have frequently instituted palmer friction massage and obtained from the skin a collection of an entire small ball of wax material. Following this the beads of sweat stand out and its reaction is highly acid. We have assumed that this was due to retained acid products in the great subcutaneous lymph space which could not escape through the ducts until the sebaceous plugs had been removed.

Insofar as the elimination of the chemical compounds, as evidenced by the crystals, is concerned, both the secretion from the apocrine and eccrine glands contain them. In the beginning we kept them separated by specially constructed rubber coffer dams.

We have had no experience with leprosy, but I believe if the cases mentioned were treated at the Marine Hospital, it will be found that a baking type of apparatus was used.

MULTIPLE PRIMARY MALIGNANCIES OF THE LARGE INTESTINE*

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A study of multiple primary malignancies tends to stimulate interest and excite speculation relative to many phases of cancer. This pathological entity is seen sufficiently often to demand consideration; in fact, the finding of two or more cancers in the same patient is no longer regarded as phenomenal. The two carcinomas may be present at the same time, or the second tumor may occur at some later date. In this presentation a discussion will be made pertaining to the frequency, etiology, diagnosis, and importance of recognition of multiple primary malignant foci of the large intestine. A few abstracts of case histories will supplement the discussion. Three hundred and six records of patients with carcinoma of the large intestine have been reviewed as a basis for this study. In 119 of these cases the tumor was in the colon and in 187 in the rectum.

When patients are reported as having multiple cancers, the question is rightly raised as to whether or not they represent multiple primary foci. Sometimes the question is quite difficult or even impossible to answer. Billroth, who is credited with reporting the first multiple primary malignancy in 1869, formulated three conditions to be fulfilled by multiple foci before their ac-

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ceptance as independent non-related tumors. These criteria are: that each tumor must have an independent histological appearance; each growth must arise from its parent epithelium; and each lesion must produce its own metastasis. Mercantor adds a fourth requirement to the effect that "there be no recurrence of the tumors after removal." These four postulates have been rather generally used in the study and determination of the existence of multiple primary malignant foci. There are exceptions, however, to these postulates. This fact has been emphasized by Cokkinis,[3] Hanlon,[4] and others. Unquestionably it would be difficult, if not impossible, to differentiate histologically many primary lesions. Could a Grade II malignancy of the ascending colon be distinguished from a Grade II lesion of the transverse?

Exceptions to the third postulate are frequently seen, for many cancers are removed before metastasis has occurred. The criterion adopted by Warren and Gates[13] is as follows:

"Each of the tumors must present a definite picture of malignancy. Each must be distinct, and the probability of the one's being a metastasis of the other must be excluded."

Phillips, the hospital pathologist, used the following pathologic criteria in the study of the specimens reviewed in the preparation of this paper: relative to location, growths must be discrete and not traceable to one another. Pertaining to structure, growths must be grossly and microscopically distinct neoplasms. Time is not necessarily important as a criterion, for multiple primary cancers may grow simultaneously. Implantation is difficult to exclude in small, superficial lesions, but not in larger ones. Microscopic structure of tumors is the best criterion, but often here mutiple lesions are found to be of the same grade of malignancy. We do not consider broken-off fragments of cancers easily implanted on a smooth mucous membrane which is in practically constant movement and often more or less covered with fecal material, mucus, or enzymes. Retrograde implantation we consider unlikely. Metastasis is not regarded as a basic criterion because it is too variable as to incidence and cell appearance.

The predilection of the patient with diffuse polyposis of the large intestine to develop cancer is well known. Multiple malignant foci of the intestine, however, occur in patients other than those with this pathologic entity. The observation of one or more discrete polyps in the colon or rectum is not infrequent in cases not regarded as having actually a multiple polyposis. This is due to the fact that the large intestine is peculiarly prone to the formation of polyps. Lawrence,[6] in seven thousand postmortem examinations, found that polyps were twelve times more common in the colon than in the small intestine. Hardy estimates that malignancy occurs in more than 40 per cent of polyps. Many believe a majority of the carcinomas of the large intestine begin in these benign adenomas, and regard all adenomatous polyps as potential cancers or precancerous lesions. This is the opinion of Lockhart-Mummery, Dukes[8] and others. A small beginning carcinoma has been seen in such tumors. Norbury[11] writes:

"If carcinoma can happen in one adenoma, it is not hard to imagine a similar transformation of a second or even several isolated polyps."

A benign polyp has been observed only a few centimeters from a malignant lesion. The tendency of these discrete adenomas to undergo malignant change is a probable factor in the development of multiple carcinomas of the large intestine.

Increased individual susceptibility to cancer is probably another etiological factor. Apparently certain persons are either born with or have acquired a type of tissue that tends to cell hyperplasia and malignant change more readily than do the tissues of others. In a discussion of this subject, Cokkinis says:

"Individual susceptibility (perhaps hereditary or familial) is the only explanation capable of general application."

The part which heredity has to do with cancer is still unsolved. The parent with the red, florid skin passes on to his children the same character of skin. Unquestionably the skin of such individuals is more susceptible to trauma, cell hyperplasia, and malignant transformation than that of the brunette type of person. Frequently patients are seen who are peculiarly prone to have skin cancer such that it necessitates their return to the hospital every few years for the removal of one or more additional epitheliomas. One such patient within the last sixteen years has been operated upon twelve times for the removal of some sixteen discrete epitheliomas, and even previous to this time he was operated upon several times. A gland dissection of the neck was performed several years ago because of metastasis to the lymph nodes of this region. Only some two months ago a patient was seen with three distinct squamous cell lesions and a basal cell cancer. Such observations repeatedly made relative to skin malignancy add additional evidence to the view that even if cancer is not

inherited, certain persons do inherit a type of tissue which more readily tends to cell hyperplasia and tumor growth than does that of the average individual. Little[7] says:

"The progeny of a cancerous mother and non-cancerous father was found to contain an excess of cancer over a general population of the same number, sex, and age group. The excess was 8.7 times its probable error. With a cancerous father and non-canerous mother the excess was 6.7."

His conclusion was that heredity plays a part in the cancer incidence in man. Genetics has proven that heredity influences the cancer incidence in mice.

The frequency of the existence of multiple primary malignancy varies in the reports in literature from 1 to 4 per cent of all cancers. Some regard its occurrence as a mere coincidence, while others maintain that it is relatively frequent and that factors other than chance are concerned in its etiology. Warren and Gates say:

"On a basis of all statistics the frequency of multiple malignancy is 1.84 per cent."

In their own series of 1,078 cancer autopsies the frequency of multiple foci was found to be 3.7 per cent. The actual percentage is probably higher than these figures would seem to indicate, for some venture the opinion that more multiple malignancies are missed than are diagnosed. While multiple primary carcinoma is regarded no longer as a particularly uncommon finding, the multiplicity of a similar type of lesion in the same organ is a relatively rare observation, for multiple cancers are encountered usually in organs unrelated by any system. In most of the published reports the colon, stomach, and pharynx, of the internal organs, in that order of frequency, are the site of multiple primary cancer. Major,[9] in 1918, reviewed the literature pertaining to this subject and recorded six hundred and twenty-eight cases with multiple lesions. The authenticity of an actual multiple primary malignancy in many of his records has been questioned. In this series, however, not a single instance of multiple foci in the colon and rectum was found. One thousand two hundred and fifty-nine cases of multiple primary malignancy were reported in 1932 by Warren and Gates after a comprehensive review of the literature. They analyzed statistically eight hundred and thirty-four cases of this group and noted fifty-five multiple malignancies of the large intestine. In their individual series of 1,078 cancer autopsies they found only two instances of multiple foci in the large intestine. Bargen and Rankin[2] register sixteen such cases, the largest individual group. Second only to this series are the reports of four patients each by Lockhart-Mummery and Cokkinis. Of authentic cases in which both growths are limited to the colon, Cokkinis in 1932 found only twenty-nine in the literature, and reported four additional cases of his own.

It is difficult even to conjecture the probability that a patient with a cancer of the large intestine may develop a second primary lesion of this organ. This is due to the small number of such cases reported and also to the fact that they are published usually as individual case reports and without a percentage relationship to other colon cases of the service. Peck, however, reviews sixty-nine cases of carcinoma of the colon; and he recounts one multiple metachronous malignancy, the interval being nineteen years between the appearance of the two lesions. Also, one hundred and thirty-one case records of cancer of the colon and rectum were studied by Abell,[1] and five patients of his series had multiple malignant foci; yet only one had a multiple primary lesion of the large intestine.

The diagnosis of multiple lesions is made first by recognizing the existence of this entity. A knowledge of this fact should be kept in mind always when examining or treating a patient with a cancer. Then, a majority of the synchronous growths of the large intestine will be diagnosed by a careful history, a proper physical examination, proctoscopic inspection, roentgen study, biopsy, and a microscopic comparison of tissue when this is available. Due consideration of the size and location of the tumors, the absence of proximity of the lesions, and the freedom from evidence suggesting that one growth is a transplant or a metastasis from the other also will aid in arriving at a correct conclusion. The time interval is of some importance when dealing with metachronous growths. Caution needs to be exercised when multiple foci exist that one be not regarded as a metastasis from the other. Particularly is this true when the tumors are metachronous in character. Sometimes the second cancer is found by accident on exploration and in some instances only at autopsy. These facts should emphasize the importance of thorough exploration when operating upon a colon lesion so that coincident tumors be not overlooked. Lahey states that we have not been sufficiently aware of the possibility of multiple lesions in the colon. The failure to diagnose the second carcinoma, or to interpret and treat it as a metastasis, would be a fatal mistake.

In this study of three hundred and six cases of cancer of the large bowel it was found that twenty-five, or 8.17 per cent, had multiple primary lesions. Sixteen patients of the twenty-five had multiple malignancies other than skin cancers, while in nine patients the second lesion was of the skin. Eight, or 2.6 per cent, had multiple primary cancers of the large intestine. Two patients had multiple primary carcinomas in the colon.

Case 1 (78475).—Mr. A. C., aged 39, entered the clinic on July 20, 1930. A diagnosis was made of carcinoma of the splenic flexure of the colon. He was operated upon August 7, 1930, at which time a primary anastomosis of the transverse colon to the sigmoid was done. A second stage operation was performed September 2, 1930, at which time a resection of the splenic flexure was done. There was some extension of malignancy into the greater curvature of the stomach, and this was resected also. The pathologist reported that a typical carcinoma, 6 cm. wide, was present and showed penetration of the wall of the colon and invasion of the adherent stomach wall to the level of the mucosa. This growth was of Grade III malignancy and had metastasized to the regional lymph nodes. He was readmitted to the hospital May 10, 1937, approximately seven years after the previous operation, at which time x-ray demonstrated a lesion of the ascending colon. He was operated upon again June 18, 1937, when a resection of the ascending colon was done. There was no evidence of a recurrence or a metastasis that could be attributed to the patient's primary lesion removed seven years previously. The pathologist reported that 7 cm. from the ileocecal valve there was a semi-annular carcinoma of the colon which had penetrated the muscle walls and extended into the adherent fat. This was a fairly well differentiated neoplasm of Grade II malignancy and was without demonstrated regional lymphatic metastasis. The patient's condition was satisfactory at the time of dismissal, July 20, 1937.

Fig. 1, Case 1
Carcinoma of the transverse colon, with extension into the stomach, first primary cancer, resected July 20, 1930.

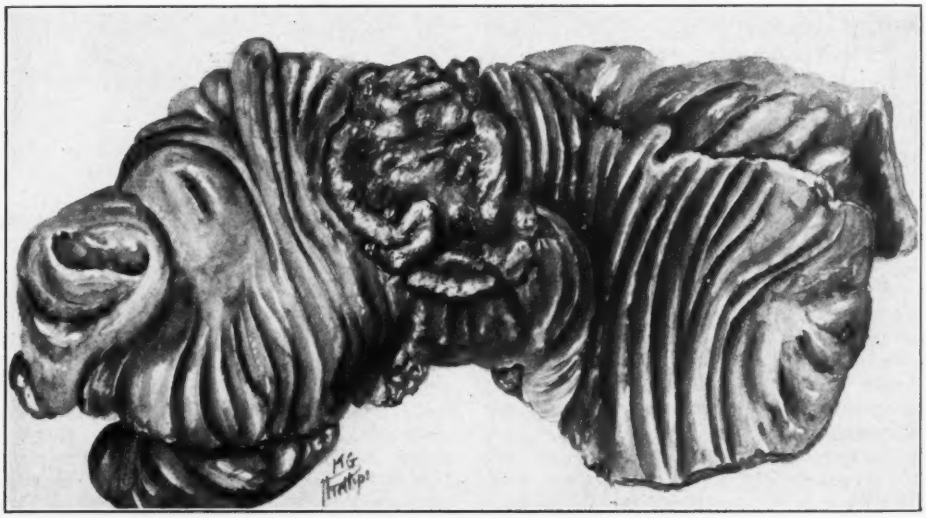

Fig. 2, Case 1
Carcinoma of the ascending colon, resected June 18, 1937, second primary cancer.

Case 2 (87108).—Mr. O. G., aged 43, entered the clinic February 27, 1932, with a lesion of the ampulla of the rectum. Biopsy revealed a Grade II adenocarcinoma. A posterior excision of the rectum was performed in July of 1932 in St. Louis. The pathologist reported that there was a carcinoma present 4 cm. above the anus, and it was of Grade II malignancy without demonstrated lymph node metastasis. He was readmitted in August, 1936, with a mass in the right upper abdomen. Upon exploration a tumor was found in the proximal portion of the transverse colon, which was resected. At this time there was no evidence of a metastasis of the rectal malignant growth. The pathologist reported that in the center of the resected colon there was an annular carcinoma, 5 cm. wide, which had penetrated the muscle coats. No glandular metastasis was demonstrated in this neoplasm, which was of Grade II malignancy. The patient's convalescence was satisfactory and he is apparently well at this time.

Case 3 (85553).—Mrs. A. C. D., aged 59, entered the hospital March 2, 1932. Sigmoidoscopic examination revealed a lesion of the rectosigmoid. A resection of the sigmoid was performed a few days later. The pathologist reported that there was a typical carcinoma, 4.5 cm. wide, in the sigmoid. In spite of penetration of the muscle wall, there was no demonstrated lymph node metastasis. This was a Grade II adenocarcinoma. There was a second distinct small growth of polypoid type, 5 cm. below the main large neoplasm. Microscopically, this was malignant because of cell changes and was diagnosed as Grade I malignancy. The patient has remained well.

Case 4 (106866).—Mr. J. L., aged 71, entered the hospital August 24, 1936. The roentgenologist reported a lesion of the transverse colon. Proctoscopic examination visualized a growth, papillary in type, 2 cm. in diameter, about 12 cm. within the rectum. Two other small polyps were observed. The pathologist reported upon biopsy of the larger lesion of the rectum that the tissue was from an adenocarcinoma of Grade II malignancy. A left rectus exploration was done, and there was found a large lesion of the transverse colon with extension into the greater curvature of the stomach and upper ileum. Resections of the transverse colon, the stomach, and ileum were performed. The pathologist reported that in the transverse colon there was an annular carcinoma, 6 cm. in width, the cells of which had penetrated the walls of the colon and invaded the adherent piece of stomach muscle for a short distance. In another direction the cancer cells had completely invaded the wall of the adherent loop of ileum to appear as a nodule in the lumen. The carcinoma of the colon was poorly differentiated and of a Grade III malignancy. In spite of this and its invasive properties, no metastasis to regional lymph nodes could be demonstrated. The patient died eighteen days after operation.

Case 5 (100197).—Mrs. M. J. A., aged 62, entered the clinic July 1, 1935. The roentgenologist reported a carcinoma of the descending colon. Upon proctoscopic examination there was visualized a lesion in the ampulla of the rectum, which involved about half of the circumference and extended along the axis of the bowel for some 7 cm. A section was taken from the rectal lesion and the pathologist reported that microscopic sections of this biopsy material showed a typical adenocarcinoma of Grade III malignancy. A left rectus exploration was performed for this patient, and a resection of the descending colon was done. The rectal lesion was not excised at this time. The pathologist reported that in the resected descending colon there was found an annular carcinoma 6 cm. wide and having by its growth narrowed the lumen to 1.5 cm. diameter. This was found to be an adenocarcinoma which had completely penetrated the walls, invaded adjacent fat, and then metastasized to regional lymph nodes. Because of the histological features it was considered to be a

Fig. 3, Case 2
Carcinoma of the transverse colon, resected in August, 1936. In February, 1932, this patient had a radical excision of a rectal lesion.

Fig. 4, Case 4
Carcinoma of the transverse colon. This patient also had a rectal lesion.

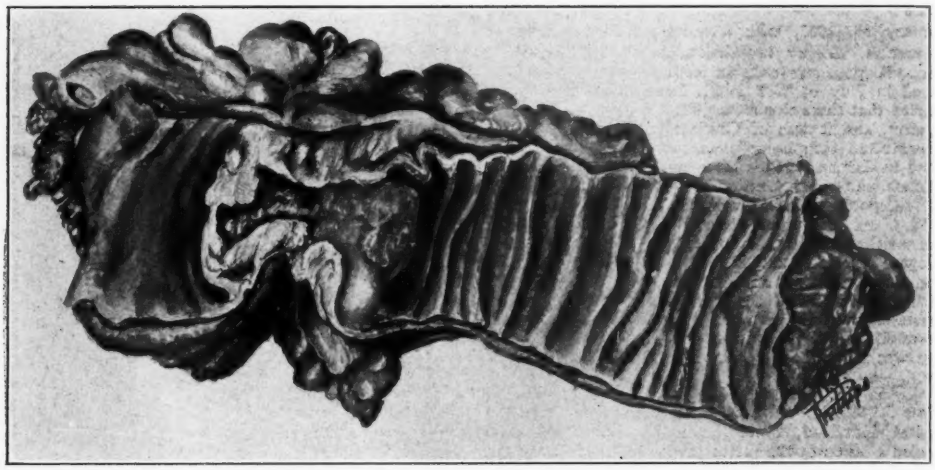

Fig. 5, Case 5
Carcinoma of the descending colon. This patient also had a rectal lesion.

Grade IV malignancy. The patient died two days following operation.

Case 6 (100933).—Mr. M. V. E., aged 25, entered the hospital August 5, 1935. Upon examination there was found a large, cauliflower mass within the rectum, also several small polyps. A local cautery excision of the tumor and polyps was performed. The pathologist reported that the first tissue from this case was a cauliflower polypoid mass 7 x 5 x 4 cm. and weighing 68 grams. Study showed this to be an adenocarcinoma of Grade I malignancy with invasive tendency. The second tissue was a rough, nodular polyp 5 x 5 x 3 cm. and weighing 32 grams. Sections showed this to be an adenocarcinoma of Grade I malignancy with invasive tendency. The third tissue consisted of two small polyps which sections showed to have present a suspicious hyperplasia. There was found no evidence of a recurrence of the malignancy upon a recent examination of the patient.

Case 7 (88770).—Mr. G. E. S., aged 35, entered the clinic November 26, 1932. There was found a large polyp about 13 cm. within the rectum. This was excised with the cautery. The pathologist reported that the tissue was from an adenocarcinoma of Grade I malignancy. The patient returned March 21, 1936, and proctoscopic examination revealed another polyp on the posterior rectal wall. This was excised with the cautery. The pathologist reported that immediate sections from this polyp gave the diagnosis of a simple polyp, but restudy at a later date revised this to a Grade I malignancy because of definite cell changes present. Structure of these distinct lesions is such that each one is regarded as a separate malignant polyp or adenocarcinoma of a low degree of malignancy. The patient has remained well.

Case 8 (63414).—Mr. A. T., aged 46, entered the clinic in March of 1936 with the complaint of recurrent diarrhea and traces of blood in the stool. Proctoscopic examination revealed three polyps on the anterior rectal wall. These were excised with cautery. The pathologist reported that one polyp was 1.5 cm. in diameter and had a base of about 1 cm. The other two were alike and of 7 mm. diameter with narrow bases. Microscopically, they were practically identical in being malignant polyps or Grade I adenocarcinomas with cells having a tendency toward invasion of their bases. A diagnosis was made of three small primary cancers of the rectum of simultaneous occurrence.

Case 9 (36029).—Mr. N. G. C., aged 49, entered the clinic in September, 1928. There was a tumor on the posterior lateral wall of the rectum. A posterior cautery excision of the rectum was done October 1, 1928. The pathologist reported that there was a carcinoma 4 cm. in diameter located 3 cm. from the anal margin and its cells had only partially penetrated the muscle coats. No metastasis of the regional lymph nodes was demonstrated from this adenocarcinoma, which was of Grade II malignancy. The patient's health remained good until November, 1933, when he began to have some pain in the chest and difficulty in swallowing. The roentgenologist reported a malignancy of the esophagus. The patient died July 10, 1935. Upon doing an autopsy, the pathologist reported that death was primarily caused by the local growth of a large obstructing squamous cell epithelioma of the esophagus with invasion of and metastasis into thoracic structures. There was a hypostatic congestion of the lungs and there was a fairly marked generalized arteriosclerosis. Careful search failed to reveal any evidence of the former carcinoma of the rectum. Anatomical position and the histological character of the rectal adenocarcinoma and of the terminal epithelioma of the esophagus make a clear case for multiple primary malignancies in this patient. There was no evidence in the abdomen of a recurrence of his rectal malignant growth.

Case 10 (18176).—Mr. J. M. C., aged 74, had a prostatic resection for a carcinoma of the prostate in 1932. The pathologist reported adenocarcinoma, Grade II. He entered the hospital again March 20, 1935, with the

complaint of rectal bleeding and pain. Upon examination there was found a large cauliflower mass just within the anus. A wide cautery excision of the lesion was performed. The pathologist reported papillary squamous cell epithelioma of Grade II malignancy.

Case 11 (30200).—Mrs. N. C. W., aged 52, had an epithelioma of the scalp removed in December, 1918. A panhysterectomy was performed in January, 1923, for adenocarcinoma of the uterus. The pathologist reported that in the fundus of the uterus there was a typical adenocarcinoma of Grade II malignancy. On April 29, 1927, an adenoma of the rectum was cauterized and 1,150 mg. hours of radium were applied. On November 22, 1927, a posterior cautery excision of the rectum was performed for adenocarcinoma. The pathologist reported that in the rectum there was an ulcerated area of 1.5 cm. diameter, and careful search through all this area revealed a small but typically localized adenocarcinoma of Grade II malignancy. The growth was limited to the mucosa and submucosa. The patient died at her home April 27, 1930.

Case 12 (34429).—Mrs. J. M., aged 49, entered the clinic on April 16, 1920. A supravaginal hysterectomy had been performed ten years previously. At this time a biopsy of the cervical lesion confirmed the diagnosis of carcinoma of the cervix. Thirty-six hundred mg. hours of radium were administered, and a cautery excision of the cervix was performed a few weeks later. The pathologist reported that tissue from the cervix showed a squamous cell epithelioma, grade undetermined. Nine years later a squamous cell epithelioma, Grade II malignancy, of one year's duration was excised from the forehead. In January of 1932 the patient was again admitted with a mass in the region of the cecum. Upon exploration there was found a tumor of the ascending colon, for which a resection of the colon was performed. At this time there was no evidence found in the abdomen of a metastasis of either of her two previous cancers. Her convalescence was satisfactory. Pathological report was that there was a large, typical carcinoma 6 cm. above the ileocecal valve which was found to have penetrated the wall to the level of the serosa. In spite of the fact that this neoplasm was of Grade III malignancy, no demonstrated lymph node metastasis was found. She died May 23, 1935, from intestinal obstruction. Autopsy revealed no evidence of a recurrence of any of her malignant growths.

Case 13 (13889).—A man, aged 54, had an angioendothelioma removed from the left leg February 4, 1933, and an adenocarcinoma of the rectum of Grade II malignancy removed March 6, 1933.

Case 14 (14173).—A man, aged 54, had an adenocarcinoma of the rectum of Grade II malignancy removed June 12, 1934, and a basal cell epithelioma of Grade II malignancy removed November 26, 1934.

Case 15 (30606).—A man, aged 61, had an adenocarcinoma of the cecum of Grade II malignancy removed March 12, 1919, and at the same time had an epithelioma under the right eye.

Case 16 (32660).—A man, aged 65, had a carcinoma of the rectum and a carcinoma of the lower lip August 4, 1924. He refused operation for this.

Case 17 (32705).—A woman, aged 51, had an epithelioma on the forehead removed September 23, 1919,

Fig. 6, Case 12
Carcinoma of the cecum. This patient had a carcinoma of the cervix fifteen years previously.

and a carcinoma of the transverse colon diagnosed by x-ray on January 25, 1923.

Case 18 (33898).—A woman, aged 52, had an epithelioma of the nose removed February 24, 1920, and an adenocarcinoma of the rectum of Grade II malignancy removed May 12, 1926.

Case 19 (45716).—A man, aged 72, had an epithelioma of the right ear and a carcinoma of the sigmoid diagnosed December 8, 1923.

Case 20 (49683).—A man, aged 67, had a squamous cell epithelioma of Grade III malignancy removed from the nose February 3, 1925, and an adenocarcinoma of the rectosigmoid of Grade II malignancy removed April 6, 1925.

Case 21 (52877).—A woman, aged 55, had an epithelioma of the nose and a carcinoma of the rectum diagnosed December 11, 1925.

Case 22 (54195).—A woman, aged 51, had an adenocarcinoma of the rectosigmoid of Grade II malignancy removed May 31, 1927, and an epithelioma of the nose diagnosed September 29, 1930.

Case 23 (61549).—A man, aged 81, had a diagnosis made of carcinoma of the sigmoid and epithelioma on the face on October 21, 1927.

Case 24 (76429).—A man, aged 65, had an adenocarcinoma of the rectum of Grade II malignancy April 5, 1930, and at the same time a diagnosis of carcinoma of the esophagus was made by x-ray.

Case 25 (98256).—A woman, aged 76, had an adenocarcinoma of the sigmoid of Grade II malignancy removed and several small epitheliomas of the face, basal cell in type, removed August 6, 1935.

Phillips, the hospital pathologist, made the

following comments pertaining to the examination of these tumors and their pathologic grading:

All tumors in this series are graded on a one to four basis of the degree of malignancy, using the well-known Broders method of histological study. Attention is paid to the degree of differentiation of the cells; to their irregularity of size, shape, and staining reaction; to the number of mitoses observed; to the degree of invasiveness shown; and to the presence or absence of metastasis. Among pathologists there is little disagreement as to the character of the lesion of adenocarcinoma of the large intestine, but as to the numerical grade assigned to a growth there is considerable disagreement, particularly in grades one and two. Final judgment rests upon the opinion of the individual pathologist as to what constitutes a benign polyp, a borderline, or a malignant one. In this series, pathologic data alone are used with chief dependence placed upon histological features. In the study of polyps we allow certain irregularities of structure, but consider demonstrated invasion of the base a malignant characteristic when coupled with other irregularities.

Our statistical study leads us to the following deductions. Certain people are either born with or have acquired a type of tissue that tends to cell hyperplasia and malignant change more readily than do the tissues of others. Heredity influences the cancer incidence in man. The presence of one malignant tumor does not necessarily immunize the patient from the development and growth of a second lesion. The patient with a cancer is more likely to develop a second lesion than is the normal individual to develop a malignant growth. A knowledge of these facts calls for even closer observation of patients who have had malignant growths. Discrete polyps of the intestine are potentially malignant and, therefore, should be removed. The possibility of more than one lesion should be kept in mind in the examination and at the operation upon the patient with cancer. Caution needs to be exercised to the end that a primary growth appearing later be not considered and treated as a metastasis of the first lesion with the unfortunate results it would entail.

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DISCUSSION (*Abstract*)

Dr. Julius Friedenwald, Baltimore, Md.—Multiple malignant lesions of the colon are not so rare as is usually supposed, though on the whole the incidence of this double lesion is not high. However, multiple malignancies occur more frequently than can be interpreted on the basis of chance alone, which can only be explained by a predisposition or susceptibility to cancer in certain individuals.

This combination is more common in the colon than in other organs of the body due to the high incidence of polyposis in this region, for it is well recognized that polypi are often forerunners of future malignant disease. These multiple lesions may occur simultaneously or develop separately often after long intervals. They are frequently separated by a considerable distance as between the rectum and cecum. It is well known that this condition occurs more frequently in females.

Recognizing that this multiple combination does occur it is wise in all instances of cancer of the rectum before considering operative procedure to rule out, by means of complete roentgenologic studies, the presence of another growth occurring in the colon.

THE SIGNIFICANCE OF INTERSTITIAL MONONUCLEAR PNEUMONIA*

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Interstitial mononuclear pneumonia has been recognized as a morbid anatomical entity since 1884, when it was described by Delafield.[1] It was not, however, until the World War when MacCallum[2] and Opie and his associates[3] reported this type of pneumonia in soldiers who died after having influenza and measles that it commanded much interest. Since this time the observations by Muckenfuss and his associates,[4] McCordock,[5] Rivers and Berry[6] and others that viruses cause a mononuclear reaction in the lung have increased this interest.

The fact that viruses cause this type of reaction has resulted in the comparative neglect of the other incitants of this morphological change. In a study of the lungs from the routine necropsy

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service of this hospital it was found that interstitial mononuclear pneumonia was present to some extent in a number of them. The apparent causes of this change were quite variable. Hence, it was thought that a discussion of all the factors that lead to this change would be of value.

Before discussing the causes of interstitial mononuclear pneumonia it should be stressed that the lung's reaction to injury is not essentially different from the cellular reaction in the other organs of the body, the differences which appear being due to the peculiar anatomical structure of the lung. The excellent morphological studies of Miller[7] have settled most of the questions in regard to the lung structure.

There is, however, one point about the lung which is not settled, namely: whether or not the alveoli are lined with epithelium. If the alveoli are not lined with epithelium, the lungs are really only tissue spaces or, as suggested by Macklin,[8] a "functional interstitial emphysema." If this is true, then what has been described by many writers as proliferating lining cells are only monocytes. If they are lined with epithelium, then the alveolar spaces are outside the body, and the epithelium is subject to damage, necrosis and proliferation just as is epithelium in general. At present, we do not find either theory thoroughly convincing. The concept, however, that the alveoli are lined with epithelium seems to be the more reasonable, so in this paper it will be followed.

Although the term interstitial mononuclear pneumonia is in fairly common usage, it seems advisable to define the term. Interstitial mononuclear pneumonia is a reaction in the lung in which the predominant type of cell is mononuclear. These cells are present in both the alveolar walls and in the alveolar spaces. In most instances the cells are either monocytes or macrophages. They arise, as has been shown by numerous workers,[9] both from the blood stream and from the parenchyma of the lung, and appear to multiply after they enter the alveoli.

In addition to the monocytes and macrophages there are varying numbers of lymphocytes, epithelial lining cells, giant cells and polymorphonuclear leukocytes. These cells are always present to some degree, but the factors which cause them to be present in either large or small numbers are at present not understood.

In any consideration of interstitial mononuclear pneumonia, one must bear in mind that if portions of the lungs are non-air-containing when fixed, the walls of several alveoli will be in apposition, thus giving the erroneous impression that the alveolar walls are thickened. To avoid this many of the workers mentioned in this paper have been careful to inflate the lungs with air before fixing.

In order to keep this paper in reasonable limits, consideration of such chronic mononuclear lesions as syphilis, tuberculosis, and fungus infections will be omitted. Also no mention will be made of the fibrosis which is commonly associated with long-standing pneumonias.

Muckenfuss and his associates[4] have given us the best description of the changes produced by viruses in the lungs. These writers, by using different amounts of the Levaditi strain of vaccinia, were able to produce pictures similar to those which occur with other virus diseases, small amounts resulting in an increase in the mononuclear cells throughout both the interstitial tissue and the alveolar spaces. This is shown in *Fig. 1.* Similar changes to these have been described by Rivers and Berry[6] and others in psittacosis and by Francis[10] in influenza. Larger amounts of vaccinia caused a necrotizing and hemorrhagic pneumonia. In producing both of these types of pneumonia, I have found that during the first 24 hours there is considerable polymorphonuclear cell reaction. Of course, when there is much necrosis there is a persistence of the polymorphonuclear cells.

Sprunt and his associates[11] have shown that results similar to those obtained by Muckenfuss and his associates[4] can be produced with certain bacterial toxins. A proliferative mononuclear pneumonia resulted from small amounts of the toxins and an hemorrhagic necrotizing pneumonia with larger amounts. The result of intratracheal injection of a small amount of staphylococcus toxin is shown in *Fig. 2* and the result of the toxic material from the Bordet-Gengou bacilli in *Fig. 3.*

Some years ago Winternitz and his associates[12] showed that similar changes resulted from small and large amounts of hydrochloric acid. In a few experiments I have found that the same results could be obtained with sodium hydroxide and snake venom. Various gases[13] also cause an interstitial mononuclear pneumonia.

All of these substances can be grouped together as protoplasmic poisons. Their reactions in all instances are similar, small amounts causing a proliferating mononuclear reaction and larger ones a necrotizing and hemorrhagic change.

Blake and Cecil[14] and Permar,[15] although differing in their description of the early stages of pneumococcus pneumonia, both observed that the reaction soon affects the interstitial tissues. The interstitial tissue is first filled with polymorphonuclear leukocytes. This is followed by the exudation of a large number of red blood cells, fibrin and polymorphonuclear leukocytes into the alveoli with resultant consolidation. Both papers, however, mention that a number of mononuclear cells are seen throughout all stages of the pneumonia. Blake and Cecil state that if the animal is killed during resolution or recovery the cells present are predominantly mononuclear. This was particularly well pointed out by Robertson and Uhley.[16] In examining sections from the lungs of patients dying of pneumococcus pneumonia, numerous areas were found as illustrated in *Fig. 4* which could not be differentiated from other interstitial mononuclear pneumonias.

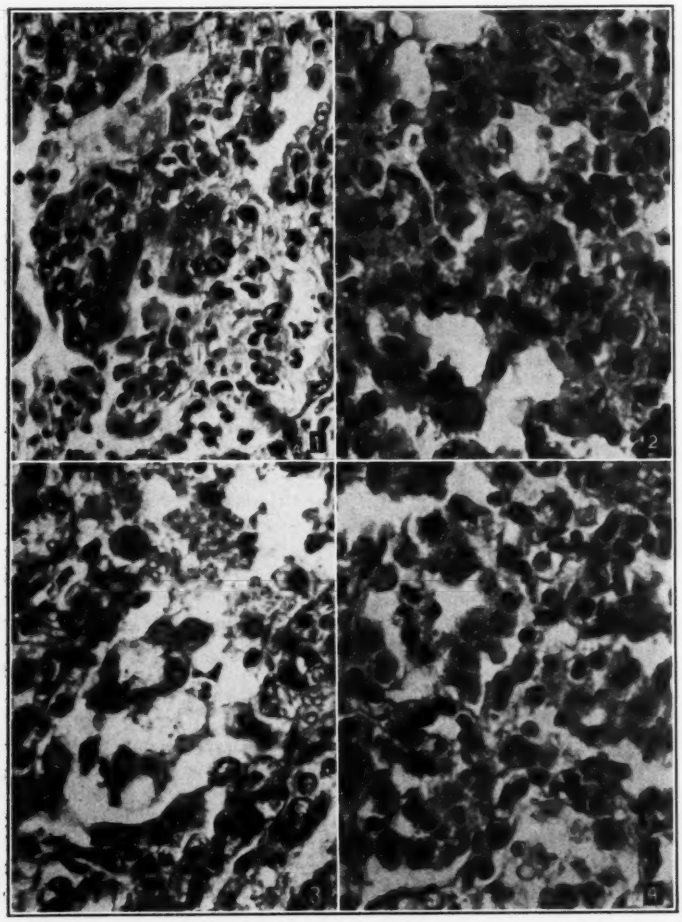

Fig. 1. Section of rabbit's lung seventy-two hours after intratracheal injection of vaccinia (x 300).

Fig. 2. Section of rabbit's lung seventy-two hours after intratracheal inoculation of staphylococcus toxin (x 300).

Fig. 3. Section of monkey's lung seven days after inoculation with virulent Bordet-Gengou bacilli (x 300).

Fig. 4. Section of human lung from a man who died of pneumococcus I pneumonia (x 300).

The cytology of other bacterial pneumonias is quite variable even in pneumonias due to the same organisms. Olcott[17] points out that a Friedlander's bacillus pneumonia may be polymorphonuclear in character, but that it may also be composed almost entirely of mononuclear cells as is shown in *Fig. 5*. Pfeiffer's bacillus also at times causes a predominantly mononuclear pneumonia as shown in *Fig. 6*. In the streptococcus pneumonias there are always some mononuclear cells present, but at times they are more prevalent. These pneumonias, like the pneumococcus ones, always go through a stage of resolution. At this time most of the cells are mononuclear.

Pinkerton,[18] in 1926, reported 6 instances of mononuclear pneumonia following the aspiration of lipoids. This work has since then been conclusively verified and MacCallum,[19] in his textbook of pathology, refers to it as "lipoid cell" pneumonia. In 1927, Pinkerton[20] further investigated this problem and found that lipoids obtained from animals would produce changes whether they were injected as neutral fats or as fatty acids, whereas vegetable lipoids

would produce no change unless free fatty acids were present. This finding has been verified by Heatly and Clausen.[21] A typical example of lipoid cell pneumonia is shown in *Fig. 7*.

Pinkerton also showed that mineral oil would produce a monocytic pneumonia. The only difference between it and that caused by the fatty acids was that no necrosis was present with mineral oil, whereas, the reaction occurring with the fat and vegetable lipoids always was associated with some necrosis.

Pinkerton offers as a possible explanation that the lipase present in the lung can hydrolize the animal fats, but is not able to hydrolize the vegetable ones. His theory, however, seems to have little to support it, as workers with enzymes find that lipases are non-specific and can act on both vegetable and animal fat equally well. Further work on the toxicity of the lipoids is needed, as it has been shown by Sabin and her associates[22] that much of the reaction to the tubercle bacillus is due to fatty acids which it contains. Ross,[23] working in this laboratory with lipiodol and staphylococcus toxin, has shown that whereas the lipiodol stimulates only the monocytes as was shown by Fried,[24] the toxin causes proliferation of the epithelial lining cells as well as the monocytes.

There have been numerous reports of studies made by various investigators on the effect of the injection of other foreign substances into the lung. Some of these are: zinc stearate[25] resulting in pulmonary fibrosis, and egg white,[26] which causes a predominantly polymorphonuclear cell reaction. Thus one finds inert substances which produce lesions similar to those produced by bacteria. Although absolute proof is not available, it is reasonable to believe that further study will reveal that all of these reactions pass through the same stages of engorgement, exudation, and resolution as the bacterial pneumonias; the only difference being that the various phases are either minimized or increased, depending on the nature of the chemical substances.

In this discussion of foreign substances one of the more common ones should be considered, chronic passive congestion. Parker and Weiss[27] have recently described this in detail. It suffices here to point out that the mononuclear

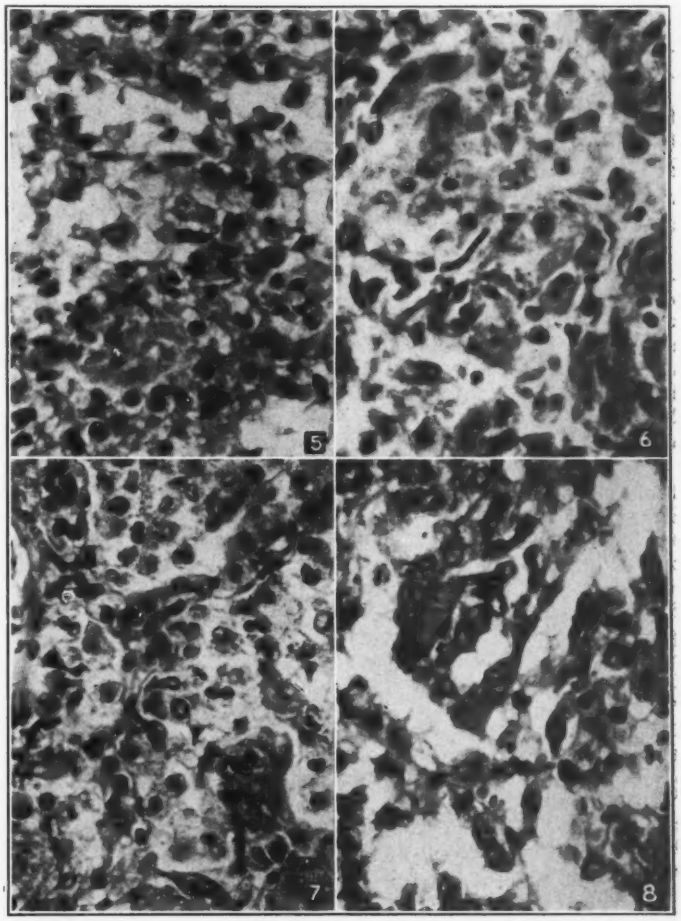

Fig. 5. Section of lung from a man who died of Friedlander's bacillus pneumonia (x 300).
Fig. 6. Section of lung from a man who died of Pfeiffer's bacillus pneumonia (x 300).
Fig. 7. Section of lung from a child who died as the result of aspiration of milk (x 300).
Fig. 8. Section of lung of a man who died of congestive heart failure (x 300).

change is similar to that occurring with other mononuclear pneumonias except that the cells are filled with hemosiderin and the blood vessels are dilated. An example of this is shown in *Fig. 8*. A similar mononuclear reaction may take place in the lung as the result either of hemorrhage into the lungs or of blood reaching the lungs from the upper respiratory tract.

Aspirated coal dust also produces a picture similar to that of blood pigment. The changes produced by the inspiration of dusts show considerable variation. The reaction depends on the toxicity of the material aspirated. Gardner[28] has shown that silicon (SiO_2) will produce changes almost identical to those caused by the tubercle bacillus.

DISCUSSION

From the above review it is apparent that interstitial mononuclear pneumonia is a phase of almost all types of pulmonary damage. It was seen that some incitants caused a predominantly polymorphonuclear reaction which persisted throughout the acute stage of disease, while in others the polymorphonuclear reaction was transitory, lasting only a short time. As the mononuclear reaction follows the polymorphonuclear one it is evident that the mononuclear cells will be present in the acute stage in some diseases and in other diseases only during the state of healing or resolution.

It is desirable to explain why the polymorphonuclear cells persist in certain instances for so much longer periods of time than others. At first sight it might appear that this distinction could be made by ascertaining whether the incitant was a bacterium or a virus, as most of the bacteria have a polymorphonuclear reaction associated throughout the acute course of the infection. The foregoing review, however, discloses that this is not true of all bacteria, particularly of those which have a toxin associated with them. Moreover, the picture is complicated by the presence of inert foreign substances which gain access to the lungs. Although the majority of these substances cause only a transitory polymorphonuclear cell reaction, there are some which cause these cells to persist for some days. Textbooks of bacteriology refer to some bacteria as having a positive chemotactic action for the polymorphonuclear cells and others as having a negative one. Giving a name to this recognized difference between bacteria does not aid us in understanding this phenomenon, but it is the best we can do as far as we can go at the present time.

Menkin[29] has recently reported that the change from a polymorphonuclear reaction to a mononuclear one is associated with a change in the pH of the tissue fluids from alkaline to acid. Further work, however, is needed to show what it is that causes this shift in the pH and its accompanying cell change. Studies on the nature of the incitant, however, will not elucidate the whole problem, since changes in the cellular response may occur as the result of changes in the host susceptibility.

CONCLUSIONS

Interstitial mononuclear pneumonia is shown to be only one phase of the lung reaction to almost all causes of pulmonary disease. The reason that this type of reaction is more apparent in one disease than another is that in some instances as virus diseases the mononuclear reaction occurs in the acute phase of the disease and in others as pneumococcus pneumonia in the stage of resolution.

Explanation of these differences awaits further work on both the chemical nature of the incitant and on the presence or absence of sensitization of the host to the particular incitant involved.

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THE SURGICAL TREATMENT OF CANCER OF THE LARYNX*

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Many millions of dollars have been spent in study and scientific investigation of the etiology and treatment of cancer, but up to the present time no definite cause for this disease has been found and no certain cure has been developed. Surgery still continues to be the most satisfactory method of treatment of cancer.

From time to time we have seen promising theories and hopeful management of malignancies fall by the wayside when subjected to the test of time. Vaccines, serums, various drugs, lead, and even gold have been tried without a specific cure being found.

At present we are passing through an era where there is extreme enthusiasm by some for the use of physical modalities in the treatment of cancer. Endothermy has its advocates. Radium is of great value, but it cannot be used in all cases.

The greatest claims, however, are now being made by the roentgenologists. With improvement and further development of high powered x-ray machines, whereby the dosage can be carefully controlled by trained technicians, there is much promise that this may in time prove to be a great advance in the palliative treatment of cancer. But until such conservative methods have demonstrated their superiority over a period of years, we must depend upon surgery.

It is now usually admitted that complete early removal of a cancerous growth by surgical means offers the best chance of cure. Good results, however, depend upon two important factors: first, early recognition of the lesion; and second, immediate elimination of the infected area by a thorough operation adapted to the particular case.

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DIAGNOSIS

The importance of the early diagnosis of cancer cannot be too frequently emphasized. Constant education of the public, more intensive instruction of medical students, and arousing the general medical profession to become "cancer conscious" will be the means of saving many patients from serious consequences. When we realize that deaths from cancer now stand second in mortality tables, having advanced from tenth place in the past decade to this alarming figure, it is a cause for concern with all of us. Over this same period of time we have seen the death rate for tuberculosis drop from second place until it is now tenth in the list, but no progress has been made in the control of cancer.

As about 4 per cent of the cases of malignancy occur in the larynx, it is a subject of vital interest to all laryngologists. The early diagnosis of carcinoma of the larynx is not difficult and should not be overlooked. It is a disease occurring most frequently in men, of adult life or old age, although cases have been reported in the young. New[1] records a case at 16 and one at 20. Clerf[2] had a patient at 21 years old, and MacKenty[3] described cases occurring at 20 and 29 years of age.

The significant symptom of cancer of the larynx is hoarseness. Any adult male developing any alteration in his voice such as weakness, huskiness, hoarseness or aphonia, should be regarded with suspicion and should be considered a potential cancer patient until his symptoms have been explained as due to another cause.

A simple indirect examination with a laryngeal mirror is usually sufficient to make out a new growth in the larynx. Carcinoma has a tendency to invade the anterior third of the vocal cord. Any roughening, irregularity, thickening or nodular mass in this region is suggestive of cancer, and a biopsy should be made. A piece of tissue may be carefully taken from this area, after which the raw surface is seared over with an endotherm. This will not result in serious complications and a positive diagnosis can thus be easily made.

DIFFERENTIAL DIAGNOSIS

The most common chronic laryngeal lesion requiring differentiation is that of laryngeal tuberculosis. In tuberculosis there is some manifestation of the general disease, because laryngeal complications are always secondary to a pulmonary lesion. The local picture is also characteristic, whereas with carcinoma having a predilection for the anterior part of the larynx,

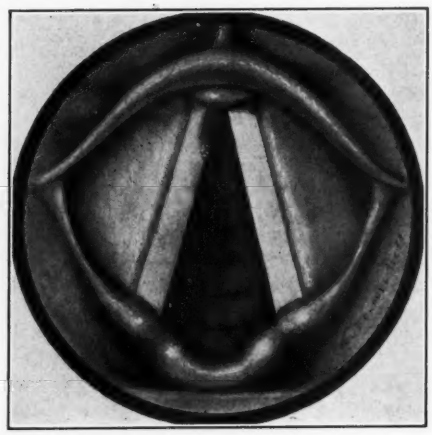

Fig. 1
Very early carcinoma of the larynx.

occurring as a nodular mass, tubercles may occur on any part of the laryngeal surface. The pathology is variable. The infection may be a single nodular tubercle, or it may manifest itself by multiple lesions. Some are edematous, others superficial or deep ulcerations with secondary infections, depending upon the degree of invasion. Tuberculosis most frequently attacks the posterior laryngeal wall, the arytenoids, the margins of the vocal cords, the false cords, the epiglottis, and even the pharynx.

Syphilis of the larynx, in my experience, has been uncommon. When it is present the diagnosis is easily made. Being a blood borne disease, it affects the laryngeal mucosa in a uniform manner. The vocal cords are equally congested. Infiltration and gummatous formation occur only in the late stages of the disease. Hoarseness often occurs in the secondary stages, but at this time there are enough general symptoms associated to make a positive diagnosis. Temperature, skin eruptions, general glandular enlargement, with a history of the primary lesion, indicate this disease. If still questionable, the use of a blood test will confirm the diagnosis.

Chronic catarrhal laryngitis with edematous lesions and ulcerated areas on the vocal cords in old people may at times prove to be a difficult problem in differential diagnosis. The responsibility for the diagnosis is great, because if the lesions are benign a biopsy is unwarranted and may result in some permanent damage to the vocal cords, while if a cancerous growth is developing the patient's life may be jeopardized by delay in making an early diagnosis. However, in these cases, there can usually be found some focus of infection in the upper respiratory tract which is the cause of the trouble. Such cases of chronic laryngitis are generally due to infection in the tonsils, teeth or accessory sinuses, and when these are cleared up the laryngeal lesion will disappear.

Any new growth occurring in the larynx of an old person should be watched carefully even though it appears benign. Papillomas have a tendency to become malignant in the aged, and their early removal is indicated.

TREATMENT

MacKenty[4] found that 98 per cent of malignant tumors of the larynx were carcinomas, 1 per cent adenocarcinomas, 1 per cent papillary carcinomas, and 2 per cent basal cell carcinomas.

The type of carcinoma most frequently found in the larynx is the highly malignant squamous cell variety, which occurs in 96 per cent of cases. Most of these patients will die within one to three years unless the growth is removed by surgical means. In a study of two hundred cases, Tucker[5] found that 72 per cent had intrinsic cancer, the type which offers a good chance of cure if operated upon early in the disease.

Cancer varies considerably in the degree of malignancy, but by proper grading valuable information may be obtained as to the type of lesion. After grading, the special operation best adapted to the particular patient can be selected, as each case must be treated individually.

Fig. 2
Type of laryngeal cancer where laryngofissure is indicated.

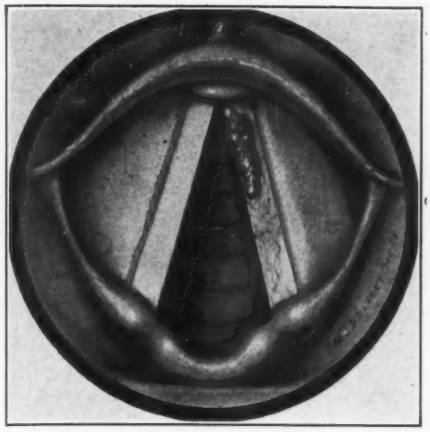

Fig. 3
A biopsy is necessary to differentiate cancer and tuberculosis of the larynx in such a case.

OPERATIONS

The removal of malignant growths within the larynx by endoscopic methods is very difficult and is not generally used.

Laryngofissure.—The most satisfactory operation for laryngeal cancer is laryngofissure. This operation is safe, gives the patient a useful voice, a free airway, can be performed under local anesthesia, and requires only a short stay in the hospital. St. Clair Thomson[6] claims that 80 per cent of suitable cases can be cured by laryngofissure. Unfortunately this operation is adapted to only a selected group of early cases, those in which the growth is limited to the anterior surface or free edge of a mobile cord, so that only a small number, about 20 per cent of cases, are recognized in time to use this conservative operation.

In discussing my paper,[7] "Laryngectomy for Cancer of the Larynx," which was read in Philadelphia February 15, 1937, Chevalier Jackson said:

"One cannot help but deplore the unquestionable fact that the presence of cancer of the larynx is still overlooked when it is in the stage curable by laryngofissure. Of the last two hundred and fifty-four patients with cancer of the larynx that have come to the service of Dr. Chevalier L. Jackson and myself at Temple University Hospital, only 23 per cent were suitable for the relatively minor and non-mutilating operation by the laryngofissure route. By this route 82 per cent of suitable cases are in the curable class. Yet there can be no worse mistake than to attempt removal of extensive or extrinsic laryngeal cancer by the laryngofissure route. Doing so has led to lack of appreciation of the great boon to humanity, or at least to the part of humanity represented by the patint with early intrinsic cancer and his family."

Laryngectomy.—For the cases with more extensive involvement, comprising about 80 per cent of the group, the more complete operation of laryngectomy is used.

The first total laryngectomy for cancer in man was performed by Billroth in 1873. From that time up to 1907, only five hundred operations of this type had been reported. Early results were discouraging, complications common, and the mortality rate was high, so that this operation made slow progress at first and was generally used as a last resort with little hope of curing the patient.

Today, we know that laryngectomy can be safely performed by modern technic so that results compare favorably with those of any other surgical procedure, the mortality rate being less than 2 per cent.

The single stage operation is usually employed. In most cases the cancerous growth can be removed at the first operation. With some patients, where there is marked dyspnea, it is advisable to perform a preliminary tracheotomy, but these cases are in the minority.

Preparation of Patient.—As this disease occurs most frequently in elderly people, consideration must be given to the patient's ability to stand the operation. Investigation must be made to discover complicating diseases which occur at this time of life, and every patient should be carefully examined and treated, if necessary, by an internist before the operation

Fig. 4
More advanced carcinoma of the larynx where laryngectomy is indicated.

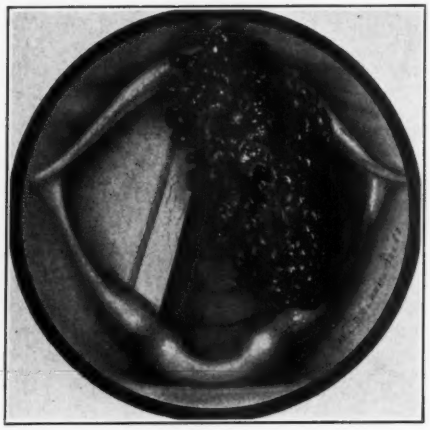

Fig. 5
Advanced stage of laryngeal carcinoma.

is contemplated. Diabetes and nephritis are common. Hypertension should be suspected. Infected teeth or other focal infections in the nose and throat should be removed. In fact, all factors which affect the patient's general resistance should be corrected before the operation is performed.

Administration of Anesthetic.—Before the perfection of rectal anesthesia, it was a common practice to perform most laryngectomy operations under local anesthesia. With the gaseous anesthetics usually employed, definite difficulties are added to the operation. The anesthetist is necessarily so close to the field of action that he is in the way. Even extended rubber tubes embarrass the surgeon in his work. Most important of all, the concentrated fumes of ether on the mucosa of the lower trachea and bronchi in debilitated patients is always a matter of concern. These complications of course can be avoided by block and infiltration anesthesia, but local anesthesia also has its disadvantages. The patient is conscious, and this is a serious handicap. It is extremely depressing to most people to learn that they have cancer, but to know that they must lose their organ of voice is a real tragedy. So to lie on an operating table for several hours meditating on their misfortune while their vocal cords are being removed produces a mental shock and vasomotor disturbance which must affect the immediate recovery from the operation and certainly prolongs the convalescence. By the use of rectal anesthesia many of these difficulties are overcome. We prefer tribromethyl alcohol and invaribly use it as a basal anesthetic. In most cases the entire operation can be completed while the patient is under the influence of this drug alone. However, if necessary, a small quantity of ether in olive oil can be satisfactorily given *per rectum* as the particular case demands. With tribromethyl alcohol the patient goes to sleep easily, quietly and quickly. This is a very important factor and one which frequently prevents the necessity of a preliminary tracheotomy, which is required if there is excitement, struggling, or a spasm of the constricted glottis, a condition associated with the excitement stage of gaseous anesthetics. With tribromethyl alcohol, the blood pressure is lowered, the breathing is quieter, and the patient sleeps for several hours, a very important advantage.

After using this method for several years, we are convinced that this is the ideal anesthetic for this operation and so far we have had no complications and have seen no bad effects from its use. There is one precaution, however, to be observed: the solution should never be given in the patient's room, but should always be administered on the operating table, because if dyspnea, due to the growth, should develop, an immediate tracheotomy can be performed more satisfactorily.

Technic.—The skin (anterior part of neck and upper part of chest) is shaved and carefully

Fig. 6
Gross specimen of Case No. 5, showing extension posteriorly.

scrubbed with soap and water. This can be done before the patient comes to the operating room if preferred. While the patient is going under the influence of the anesthetic, the desired area is cleansed with alcohol, ether, iodine or another antiseptic solution, the application depending upon the choice of the operator. The neck is extended as much as possible and the necessary draping arranged. Suction, with suitable small tubes, should be in good working order. Naturally, a complete tracheotomy set should be at hand with the other required instruments.

Incision.—Particular attention should be paid to the preliminary skin incision. I prefer a crescentic incision on the right side of the neck. Beginning above, near the midline at the highest point of the right thyroid cartilage, it is extended downward and outward until the central part of the incision is on a line with the inner margin of the sternocleidomastoid muscle. From here the incision is carried downward and inward to the midline on a level with the first tracheal ring.

Such an incision, to my mind, has several advantages over the customary T-shaped incision. The most important feature of the crescentic incision is that there is less weakness in the midline of the throat, where strength and support are essential after the larynx has been removed. Infection is less likely and healing is more rapid. On account of lessened traumatism and undisturbed blood supply over the esophageal region, fistulas do not develop frequently. The larynx is easily exposed and satisfactorily delivered. There is less scarring with a final result of little deformity in the conspicuous midline of the throat. If desired, a cutting endotherm may be used for cutting and dissecting throughout the operation. Such an instrument causes less bleeding and may lessen the chances of metastasis by searing over raw surfaces. However, this is a matter of choice.

The fascia and attached muscles are now cut and pulled aside and the larynx carefully skeletonized. All bleeding points should be tied off and the larynx packed around with sterile gauze. The greater cornua of the thyroid cartilage are now pulled up and severed near their ends. The larynx is then allowed to return to its normal bed. The thyroid ligament is now cut, separated from the trachea, and pulled aside. The upper end of the trachea is freely exposed and a clean transverse incision is made through the trachea down to, but not across, its posterior surface. At the posterior wall an elliptical or tongue-shaped incision should be carried upward, sufficient in size to make a satisfactory mucosal flap. This flap is important, as it strengthens the fixation of the tracheal stump and prevents irritation of the thin esophageal wall by the tracheotomy tube. The patient's head is now lowered to prevent blood and mucus from getting into the trachea and bronchi. An aspirator should be constantly used by an assistant to prevent such complications, for it is difficult for a patient to cough out secretions when once the trachea is opened. If desired, a large tracheotomy tube can now be inserted into the trachea and packed around with vaseline gauze. However, this can be deferred until later if the assistant is on his job.

After the trachea has been detached as described, the lower anterior end of the larynx is grasped with a volsellum forceps and lifted up. Now very carefully the posterior wall of the trachea is separated from the anterior wall of the esophagus; caution is necessary here, because the wall of the esophagus is very thin and a perforation will cause a fistula. This dissection is carried upward until the lower end of the trachea can be lifted out of its bed and a saline pack placed posteriorly. The trachea is now allowed to drop back into its natural position.

My next step is a slight deviation from that usually employed. Several mattress sutures of chromic catgut are inserted through the outer wall of the esophagus at the upper end in a line where the trachea is to be cut from the esophagus. The object is to do all possible work and manipulation before the esophagus is opened so as to prevent as much infection and contamination of the wound as possible. The sutures are also helpful in lifting up the larynx and later in closing over the esophageal opening. The larynx is now entirely separated from the esophagus and the raw edges of the esophageal mucosa are cauterized to prevent possible infection. From this point on there is danger of contamination from the opened esophagus, but to prevent as much of this as possible, a sterile saline pack is inserted into the end of the esophagus from without.

An assistant now passes a small rubber feeding tube through the nostril and pharynx and down to the central part of the esophagus for future feeding. The tube is held above by adhesive tape attached to the face. The assistant now pulls the gauze pack up and out through the mouth and not through the wound.

The cut edges of the esophagus are inverted

and the mattress sutures brought across and tied. The closed opening has the appearance of a T. Several smaller interrupted sutures may be necessary to close any exposed points, as it is very important to have a tight wound to prevent leakage and fistula formation. All gauze sacks should now be removed and a final inspection made to see that all bleeding is controlled and that the entire wound is thoroughly dry. The cut end of the trachea is brought up and fixed to the skin by silk sutures. The surrounding skin edges are inverted so as to form a smooth surface, which on healing will give a good cosmetic result; they are extended sufficiently so that they will remain open after contraction and thus make it unnecessary to wear a tracheotomy tube permanently.

Closure of the wound adjoining the tracheal opening above is most important. An effort should be made to establish a firm bridge of tissue which will heal quickly, so as to prevent drainage from above from entering the trachea. Muscles and fascia should be carefully closed over in this area and securely sutured to insure close approximation of the tissues and to prevent pocket formation. A long braided silk suture on a large cutting hand needle, carried through the skin into the deeper structures across this bridge so as to come out on the opposite skin surface, gives retention and support to this important area.

The next step consists in closing over the esophagus. The related neck muscles and fascia are now carefully approximated and sutured in order to form a cover and a strong support to the anterior wall of the esophagus. Close apposition of this tissue over the incised area greatly aids rapid healing and lessens the chances of fistula formation.

Provision should be made for the insertion of three or four small rubber drainage tubes. Small tubes are as satisfactory as the larger ones and give sufficient drainage unless infection should develop. These tubes should be left long enough to extend out through the dressings.

The skin wound is now closed by interrupted silk sutures. Along the line of incision a final application of iodine may prevent skin infection.

Vaseline rubber gauze is used to cover the wound and a perforated piece is placed under the tracheotomy tube, which is finally adjusted and secured by tapes around the neck. Gauze handkerchiefs are placed over the wound and are held in place with a roller bandage.

After-treatment in Laryngectomy.—The after-treatment of a laryngectomized patient is almost as important as the operation.

Exacting vigilance is required with every case. The resident and nurse must be made to realize how much depends upon them for the patient's recovery. While returning from the operating room the patient's head should be lowered. A suction machine should be placed at the bedside for immediate action and should be used at all times when secretions accumulate in the trachea and bronchi. This exudate can be aspirated with a small curved cannula; this procedure will relieve the mucosa of infected material which is often the cause of one of the chief complications, bronchopneumonia. Attention to this factor must be observed throughout the patient's convalescence. Dressings should be changed twice daily until the wound has healed. Iodine solution applied to the skin incision will prevent infection and stimulate healing.

In these cases proper feeding is essential. Concentrated liquids should be administered at frequent intervals through the feeding tube, to build up the required resistance. At the end of a week or ten days, the feeding tube can be removed and some sterile water can be taken by mouth as a test. If an esophageal fistula is present, the tube should be reinserted until healing is complete.

Complications.—Hemorrhage, usually considered the chief cause of anxiety, should not occur if the vessels have been carefully tied off at the time of the operation. It has not developed in any of my cases.

Bronchopneumonia can also be prevented by regular aspirations of secretion with a suction outfit. The patient should also be forced to change his position frequently and should be allowed to sit up in bed at intervals during the day.

Fistula formation, a common complication with the T incision, is less likely to occur if there is strong support over the esophageal incision, as employed with the technic described. If a fistula does develop, it is of no serious consequence and usually heals in a reasonable time, but if persistent, it can be closed under local anesthesia.

Results.—Laryngectomy, when performed by modern surgical technic, compares favorably

with other major procedures. The operative mortality has been reduced from about 50 per cent in the earlier days to around 1 to 2 per cent at the present time.

SUMMARY

(1) The surgical removal of cancer still continues to be the most satisfactory method of treatment of this disease.

(2) Successful surgery depends a great deal upon getting at the patient as soon as possible after the infection has started.

(3) The importance of the early diagnosis of cancer should be stressed at every opportunity.

(4) In about 20 per cent of early cases the conservative operation of laryngofissure can be used. Cures in these cases are reported as from 80 to 85 per cent.

(5) Laryngectomy is a safe surgical procedure when properly performed and compares favorably with other surgical operations. The mortality is from 1 to 2 per cent. It is to be recommended where laryngofissure cannot be performed.

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DISCUSSION (*Abstract*)

Dr. M. F. Arbuckle, St. Louis, Mo.—When we convince the medical man that he is permitting his patient to take unnecessary chances with his life by medicating his cough or hoarseness without laryngeal examination, the mortality rate from laryngeal cancer will be reduced.

As was pointed out, a laryngeal mirror usually is all that is required to establish the presence of a lesion in the larynx, and generally speaking we may by consideration of the clinical picture as a whole, and the appearance and distribution of the local lesion, be able to establish the diagnosis with a fair degree of accuracy. In some, however, this is far from true, even with the use of various diagnostic aids. Biopsy should always be made when the question of malignancy has been prominently suggested, even though other disease such as tuberculosis or syphilis be suspected. I have never seen harm follow biopsy, and have never cauterized the base. Sir St. Clair Thomson relates his experience with a case which came home to London from India after biopsy and six weeks or three months after biopsy was successfully operated upon by laryngofissure for laryngeal cancer. As to the method of choice for treatment of cancer of the larynx: if according to Sir St. Clair Thomson's classification the disease is strictly intrinsic, surgery is my choice.

If it is extrinsic, subglottic or mixed, which means glandular involvement, the choice of treatment is not easy. Notwithstanding the great value of laryngectomy and the brilliant results obtained in many instances, the fact remains that every surgeon dealing with these cases is bound to admit that the percentage of recurrence is distressingly high. In addition to these, we see cases in which at the first examination the disease is already so far advanced and so widespread that surgery is contraindicated. Nevertheless, these as well as the operable cases demand and require treatment.

Five years ago surgery plus radiation would have been my answer, but even within that time such tremendous strides have been made in the field of radiation therapy that the most conservative have been obliged to take stock of the situation and change their mind somewhat at least, whether or not they admit it.

We all know that some cancers grow and spread in spite of irradiation, but all who have tried to see have been gratified to note that an increasing percentage of cancers are now being successfully treated by irradiation. With this in mind, it seems impossible to prophesy what the developments of the immediate future may hold in store for us. It seems to me, therefore, that by a continuous effort on our part we must try to see these cases early; that when seen the diagnosis must be established with certainty, which means by microscopic examination of a specimen of the actual tumor itself. If and when the diagnosis is cancer, we must employ that form of treatment with which we may destroy the cancer without destroying the patient, whether it be surgery or radiation or a combination of these.

Dr. Kichmond McKinney, Memphis, Tenn.—Laryngectomy in itself is not a difficult operation, but a tedious one. Two very important conditions in the operation are drainage and anesthesia. Drainage need not consist of the extensive placing of tubes, as practiced by some operators, and I notice that Dr. Looper contents himself with about four drainage tubes. Some time ago I saw shown at our local society of ophthalmology and otolaryngology a moving picture depicting a laryngectomy, and the bloody field was criss-crossed with drainage tubes, so that it looked like a veritable *chevaux-de-frise*. Tubes at four points, two above and two below, are sufficient. The anesthetic used is very important. I prefer tribromethyl alcohol, with 2 per cent procaine hydrochloride as an adjunct. The first laryngectomy that I ever did was with 2 per cent procaine alone, but the tribromethyl alcohol gives one a somnolent and therefore quieter patient. The closure of the esophageal opening must be carefully and thoroughly done. I lost a patient through breaking of the sutures and infection. Good drainage, with a nurse attending the patient continuously for at least 48 hours after operation, having a suction pump handy to remove the secretions, is essential.

In recent years I have been turning more to thyrotomy and removal of the diseased cord when the involvement is not extensive. Cases seen early, when the growth is confined to only a portion of a cord, do satisfactorily by this less extensive method. I have had some very

happy results with laryngofissure, and certainly would advise its use when the growth is confined to a cord and small.

Dr. Gabriel Tucker, Philadelphia, Pa.—Dr. Looper has demonstrated a most effective technic for laryngectomy, and I think he has brought the matter of a small incision to our attention very forcefully and has demonstrated the excellent results that can be obtained with it. I have been very much interested in his paper and his results and wish to compliment him on his presentation. There is nothing to add or criticise in his work. I am sure that it will be effective in stimulating the early diagnosis and surgical cure of cancer of the larynx.

Dr. Murdock Equen, Atlanta, Ga.—Dr. Looper has again brought to our attention the fact that the salient feature of cancer of the larynx is hoarseness. It is only when this is generally known that our results will be more satisfactory and more lives will be saved.

Dr. Looper has varied the type of incision from the usual T-shaped one. This new procedure does not seem to me to afford as much exposure as the old. The patient certainly has less scarring, but to an individual who has undergone a total laryngectomy I do not think this would amount to much.

The treatment of a patient with a laryngeal tumor is still subject to a great deal of discussion. I have divided tumors of the vocal cords into two groups: those in which the cord is freely movable and those in which it is not. In the first group, with the patient's head in a Lynch suspension apparatus, the growth can be removed with sharp dissection and cautery. In the second group, when the cord is not freely movable, total laryngectomy in my opinion is the operation of choice. The percentage of apparent cures in my hands as well as in those patients that have come under my observation from other clinics is much in favor of a total laryngectomy over a thyrotomy. This is due evidently to the extensiveness of the growth which could not be dealt with either by dissection from above or by thyrotomy.

Dr. H. L. Kearney, New Orleans, La.—I wish to call your attention to preoperative preparation, especially from the standpoint of oral hygiene, in these cases. The edentulous patient presents no particular problem, but the patient with teeth, even if he has only one, may have an important focus of infection which should be treated and healed before operation. Further, any patient with teeth harbors the organisms of Vincent's infection. It is my practice in any severe, foul smelling, postoperative infection after laryngectomy to give a small dose of neoarsphenamine, because Vincent's infection may be playing a part in the disturbance.

I prefer general anesthesia in laryngectomy and like the tracheal insufflation apparatus devised by Dr. Gabriel Tucker for this purpose.

Dr. Looper (closing).—The importance of early diagnosis of cancer of the larynx has been given the consideration it deserves, because early recognition of the lesion means a better chance of cure. The discussors also appear to agree unanimously that surgery is still the method of choice in treating cancer of the larynx.

I have about discarded the use of the endotherm in preference to dissection with a knife, as the knife makes a cleaner incision which heals more quickly and gives a better cosmetic result.

PROPHYLAXIS OF INFLAMMATORY CONDITIONS IN THE FEMALE BREASTS*

By EARL CONWAY SMITH, B.S., M.D.
New Orleans, Louisiana

The purpose of this study is to point out the real need of preventing diseases of the breasts, and to outline a plan whereby this can be accomplished. Almost universal is the opinion that when an abscess begins, the end result is suppuration. The histologic structure of the breast is such that suppuration is usually deep, and causes much destruction of tissue, necessitating operative relief, and many times rendering that breast incapable of its normal physiologic function.

This study embraces 250 private cases, several hundred charity cases, and work extending over a period of eight years, together with helpful suggestions from the invaluable literature accumulated through the untiring efforts of other physicians who have realized the great need for prophylactic rather than curative measures. Prophylaxis of inflammatory conditions in the pregnant and puerperal woman will be considered.

The approach is therefore made by studying the etiology and development of the disturbances, and some of the ways in which an otherwise normally functioning gland may be converted into a pathologic one.

The physiologic approach to prophylaxis can be had only after a thorough and comprehensive study of the anatomy of the gland, stress being laid on the preservation of all the circulations, the blood, the lymph, and milk. Proper circulation will assure normal function of the gland at all times, and maintenance of the highest degree of tissue resistance.

ETIOLOGY

Approximately 85 per cent of breast abscesses are associated with pregnancy.

It is generally known that inflammatory conditions occur mostly in the postpartal or nursing stage. They do not occur often during pregnancy, less often in the non-pregnant state, early infancy, and at puberty. Primiparas are more

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often affected than multiparas: first, because their breasts are more easily injured, the tissues being more tender and much less resistant to the tugging force of nursing. Also, primiparas are, as a rule, ignorant of hygienic rules. Infections are more likely to develop in the first month of lactation and more especially at the beginning; 50 to 75 per cent of all breast infections occur in this period. Again, infections are likely to develop after the sixth month postpartum, when the baby begins to develop the incisor teeth, and again on weaning the child. It is indeed remarkable the frequency of puerperal mastitis in which both breasts are involved (15 to 30 per cent).

(a) Organisms from breast fluid[3]	Per Cent Incidence
(1) Staphylococcus albus	86
(2) Streptococcus	2
(3) Sterile	14

It was first proven by DeLee[4] that nearly all breasts contain *Staphylococcus albus*. Therefore, 85 per cent of all breasts are potential reservoirs of infection. All that is needed is an activator.

(b) Organisms from breast exudate[3]	Per Cent
(1) Staphylococci	
Albus	100
Aureus	23
Sarcinal	14
Citreus	3
(2) Streptococcus	25
(3) Micrococcus tetragenous	2
(4) Colon bacillus	
(5) Gonococcus	
(6) Typhoid bacilli	
(7) Tubercle bacilli	
(8) Spirocheta pallida	
(9) Vegetable parasites	
(a) Ray fungus	
(b) Blastomycetes	

PREDISPOSING FACTORS TO INFECTION

(1) Age. More susceptible during lactation, at new born period and during puberty.
(2) Improper strapping of breasts (*Fig. 1*).
(3) Maceration due to sucking.
(4) Fissures and abrasions predispose to lymphatic infection.
(5) Malformation of nipples.
(6) Lack of cleanliness, decomposition of milk, and cutaneous secretions in folds and crevices of nipple favor infection of nipples, and in ampullae of ducts; unclean breast pump, nipple shields, clothing, and so on.
(7) Infection of the baby's eyes and mouth.

Schalck[5] found in the mouth of newborn the following organisms:

Staphylococcus	80 per cent
Streptococcus	52 per cent
Coli	32 per cent
Pneumococcus	16 per cent

CAUSES OF INFLAMMATORY CONDITIONS

(1) Trauma
(2) Erysipelas
(a) face
(b) breast
(3) Eczema
(4) Impetigo
(5) Sore throat (hematogenous)
(6) Imperfect involution after lactation
(7) Puncture wounds
(8) Tuberculosis of breast. A tuberculous mother should not suckle her child. A healthy child should not suckle a tuberculous mother. The breast should be rendered inactive as quickly as possible. Injury, by all means, should be avoided.
(9) Syphilis of breast. This can be prevented by taking a complete history and physical examination, including repeated blood Wassermanns at intervals, if necessary, of mother, father and child

Fig. 1
Improperly applied support. Note (1) tape in baby's mouth; (2) soiled areas.

(nurse if necessary) with proper treatment immediately.

(10) Gonorrhea of breast. Careful complete examination of mother, father, child, nurse, and attendants if necessary, to be certain they are free of the disease. The disease should be treated actively. An infected child should be isolated until the disease is cured; likewise to be absolutely sure, a mother infected with gonorrhea should not suckle her child until she is cured.

(11) Typhoid mastitis can be prevented by typhoid inoculation of the mother.

(12) Vegetable parasitic infection of breasts. Mothers should be advised against chewing or sucking grasses. The mother should be isolated and the disease treated promptly, nursing to be resumed only when disease is cured.

PORTALS OF ENTRY OF ORGANISMS

(1) Milk ducts, most common
(2) Lymphatics
(3) Blood stream, sore throat; septic abortion (rare)
(4) Direct route, puncture wounds (rare)

The Development of an Abscess.—Most abscesses are preceded by a crack or fissure of the nipple. The organisms on the body are nonvirulent until induced in the proper medium as a crack or fissure, they become virulent, passing into the milk ducts, or lymphatics, to the milk, which is a favorable culture medium for growth of pyogenic organisms. The milk curdles, blocks the ducts, causing further stagnation of secretions, swelling and pain, as a result of which the organisms pass through the milk curd to the interior of the ducts, the milk being infected. The whole lobe becomes involved. Absorption takes place, the glands in the axilla become enlarged and painful, with final local and systemic reactions.

CLASSIFICATIONS OF COMMON INFLAMMATORY CONDITIONS OF THE BREAST[6]

(A) *Acute:*
- (1) Simple engorgement (not inflammatory)
- (2) Fissure around nipple
- (3) Ulceration of and around nipple
- (4) Abscess of areolar sebaceous gland
- (5) Sub-areolar abscess
- (6) Cellulitis
- (7) Galactophoritis
- (8) Breast abscess
  - (a) Intralobular (parenchymatous)
  - (b) Interlobular (interstitial)
  - (c) Combination A and B
  - (d) Retromammary (A and B and also as from infection of ribs)

(B) *Chronic:*
- (1) Chronic mastitis, with or without cyst formation
- (2) Chronic abscess, discharging sinus
- (3) Chronic inflammatory conditions due to syphilis, tuberculosis and vegetable parasites other than bacteria

(C) *Malignant* (Not inflammatory)

Aftermath of Infection.—Tissues and excoriations can usually be treated and cured. It must not be forgotten, however, that mastitis frequently appears 10 to 14 days after the healing of a fissure, a practical point to be remembered when the question of nursing arises. Since infection of the parenchymatous or interstitial structure almost invariably results in suppuration, necessitating surgical drainage, there is always a certain amount of actual destruction of tissue, and many times this is so extensive as to render the organ of little or no value for further use.

From the foregoing one can easily see the rationale and importance of prophylaxis of breast infections.

Breast, Antenatal Period.—Since more than 95 per cent of all infections of the deeper structures of the breast have portals of entry in or about the nipple, this is the most important point to be kept in mind. One must leave the normal nipple alone. Treatment for depressed, flat, or inverted nipples should be instituted very early to avoid too rigorous treatment in the later stage of pregnancy, which in itself might cause injury and infection. Gentle traction of the nipple with the fingers, using cocoa butter to soften and avoid friction, mild suction traction with vacuum hand pump, or a combination of the two, will correct by far the majority, excusing actual pathologic conditions (retracted). Should an inflamed nipple occur, look for the fissures, cracks, or maceration.

Simple rules to be observed as follows:

(1) Proper support (*Figs. 2, 3, 4, 5, 6, 7*) must be given the breast. This does more good than anything else in my experience.

(2) Treat with 2 to 5 per cent silver nitrate or with pure carbolic acid, and then apply boric acid ointment.

The breasts should be carefully inspected at frequent and regular intervals during this period. Very large breasts have a tendency to sag or become pendulous due to congestion any hypertrophy, and as such are often potential cases for cracked nipples or fissures, especially cracks circumscribing the base of the nipples. This type of breast should be supported by correct strapping (*Figs. 2, 3, 4*), or with a properly fitted brassiere (new type, *Figs. 5, 6, 7*), which should be applied at the beginning of pregnancy

Fig. 2
Ideal method of support is used. Same case as Fig. 1. Note (1) baby nurses without difficulty; (2) sterile nipple pad protects left nipple.

and worn until the baby is weaned. This allows for proper circulation of gland secretions, lymph and blood, especially in the nipple where the blood vessels are delicate. At the same time, injury is less liable to occur. Proper support, then, of an apparently normal breast and nipple, assuring proper circulation of all the fluids of the breast, is all that need be done during the prenatal period.

Breasts in the Postpartal Period.—The breast during the postpartal period deserves special mention. Seven of the most frequent complications are: maceration, blebs, fissures, abrasions, engorgement, caked and abscessed breasts. By far, the majority of these can be prevented by using common sense,[7] cleanliness, protection, support and by regular nursing. The baby should not be allowed to nurse an empty breast or when the milk begins to fail. Complemental feeding prevents unnecessary tugging at an empty breast. All breasts are properly supported by adhesive tape or a properly fitted brassiere on the first day, again insuring proper flow of all circulations, the milk, lymph and blood at all times. A saturated solution of boric acid, or cold cream, is used to cleanse the nipple before and after each nursing. A sterile pad of gauze or absorbent cotton is applied over the nipple to absorb milk and secretions and for protection. These pads are changed as often as they are soiled. The mother should be informed and well instructed as to daily hygiene of nipples and breasts, and should tell the physician when the breasts begin to fill, and the very beginning of soreness of the nipples and pain in the breasts. At this time boric acid in an ointment is applied, covering with sterile pad, removing before the next nursing, repeating until they are no longer painful. When milk is in excess, breast pumps are not necessary as proper support allows the milk literally to flow out of the nipples.

Simple rules to be observed are as follows:

(1) Make sure that the nipple is usable.
(2) Maintain proper support to breasts (*Figs. 2, 3, 4, 5, 6, 7*).
(3) Treat abnormal conditions at their very onset, to avoid progressive infection resulting in abcesses.
(4) Cleanliness and careful observation.
(5) Regularity of nursing.

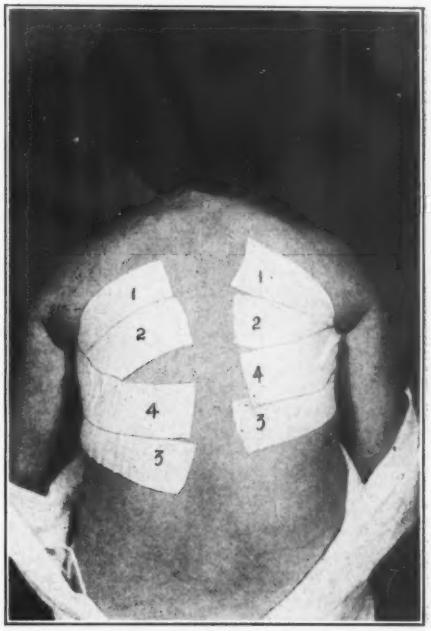

Fig. 3
Back view of ideal breast support, showing correct application of adhesive tape to make support.

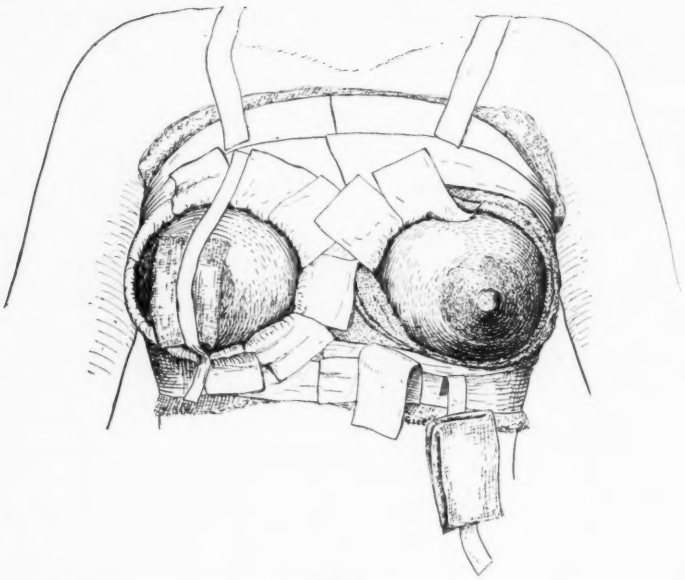

Fig. 4
Ideal breast support, front view, showing (1) construction; (2) sterile nipple pad.

(6) The child does not suckle from an inflamed nipple or breast. A breast pump at the regular feeding interval is used with caution, and the milk is discarded.

(7) Instruct the patient to inform you of any abnormality of nipple, breast or baby's mouth as soon as noted. Do nothing to the child's mouth unless there is infection, and then it should be treated, but it should not nurse until cured. Proper support and breast pump are used until the child is able to nurse.

PROPHYLAXIS OF COMMON DISORDERS OF THE BREAST

(a) *Simple Engorgement.*—This is the commonest breast disorder due to sudden filling of the breast with milk with subsequent lymphatic and venous stasis. Ordinarily breast abscesses do not follow this condition, but there is impairment of all circulatory systems, and if this is true, then it must be admitted that subsequent infection is possible and liable to occur; and particularly is this true if the breast sags, and most of them do, injury being more likely. My procedure in these cases has been:

(1) Maintenance of proper support (*Figs. 2, 3, 4, 5, 6, 7*) before engorgement, and hence before they are painful.

(2) A hands-off policy. I have not found it necessary to massage such cases.

(3) Saline cathartic may be given.

(4) Restriction of fluids.

(5) Ice bag may be applied to relieve pain, but usually this is not necessary.

(6) Tight binders are not used at any time. Remember that lymphatic and venous stasis, plus milk stasis exists, and tight binders only add to further stasis.

(b) *Drying up of Milk.*—If for any reason one is desirous of drying up the milk, unless certain precautions are taken, the breasts will become engorged with subsequent lymphatic and venous stasis; and here again lies a suitable medium for infection. The following measures are essential:

(1) Proper support of the breasts until they have diminished about 50 per cent in size.

(2) Liquids in the diet are reduced 50 per cent or more.

(3) A saline cathartic is given at 2 or 3 day intervals.

(4) Avoid firm compression of breasts.

(5) A hands-off policy again (no massage).

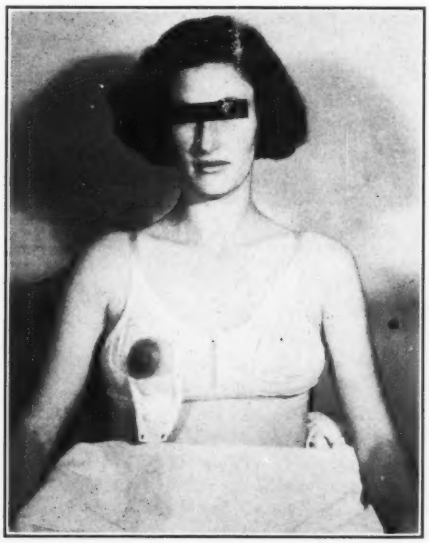

Fig. 5
New type brassiere, front view. Note (1) exposure of nipple; (2) nipple flap with sterile pad; (3) hooks on flap for closing opening; (4) zipper; (5) breast supported in correct position.

Fig. 6
New type brassiere, front view with baby nursing. Note (1) no interference in nursing; (2) ease with which baby nurses.

(6) No drugs need be used.

(c) *Caked Breast.*—An engorgement of one or more lobules due to

(1) Simple congestion

(2) Occlusion of one or more lactiferous ducts

(3) Injury

If the breast is not painful, strap properly and leave it alone. If it is painful,

(1) Give proper support to establish circulation

(2) Perhaps ice bag

(3) Hands-off policy

(d) *When Infection Seems Inevitable.*—After treating one of the above-mentioned conditions, if results are not obtained, the condition seeming to progress, more vigorous treatment must be instituted in an effort to abort it or localize the infection to avoid spreading. Hot applications of magnesium sulphate are employed, of one-half hour duration every two hours with alternating applications of ice bag for one-half hour every two hours for twenty-four hours. If improvement results, one would feel justified in continuing the treatment. If not, surgical drainage is resorted to immediately, without waiting for fluctuation, for by the time an abscess of this type has pointed, as a rule, many lobes are involved with consequent serious destruction of tissue. Early and free incision and drainage also prevents in most instances multiplicity of abscess formation, proper support being maintained always.

I have thus far referred to proper support of the breast many times. Just what does this mean, and how is it accomplished and maintained? There are many ways in which this can be done,[8] by use of slings, adhesive tape, binders of cloth or elastic; and all may be of value when properly applied. Too often when good results are not obtained, it is because of failure to maintain the breast in a position to allow proper flow of all the circulating fluids which are necessary for its proper function. The method that I shall describe is one I have used successfully for the past eight years, and in my hands it has proven most successful. This method preserves the normal physiologic functions of the gland.

(A) Articles required

(a) Adhesive tape, 2 inches wide

(b) Gauze, sterile, in square packs 6x6x0.5 inches.

(c) Bandage scissors.

(B) Procedure and technic (*Figs. 3, 4*)

(1) The patient must lie down on one or the other side. If on the right side, the left side or left breast is strapped first, or *vice versa.*

(2) With the patient on the right side, the left forearm and arm extended over the head, the

Fig. 7
New type brassiere, back view. Note (1) elastic adjustment; (2) hooks for fixation.

breast falls toward the midsternum. This breast is then held securely in this position, being somewhat elevated at the same time by an assistant. Pads of sterile gauze are placed about one-half inch thick to surround the breast completely and in the axilla. Four strips of adhesive tape, each about 18 inches long, are needed for each side. Application of first strip, No. 1 (*Fig. 3*) begins about one inch lateral to the vertebral column, crossing the middle one-third of the scapula through the axilla around the lower aspect of the breast, about 1½ inches away from the nipple, and is attached temporarily to the skin of the chest wall below the right breast. Strip No. 2 (*Fig. 3*) begins about one inch lateral to the vertebral column just below strip No. 1 and passes over the lower one-third of strip No. 1, and is likewise attached temporarily to the skin below the right breast. Strip No. 3 (*Fig. 3*) begins 1 inch lateral to the vertebral column over the lower three or four ribs, and is applied diagonally across the upper part of the breast about 1½ inches away from the nipple, the end of which is attached to the skin above the right breast temporarily. Strip No. 4 (*Fig. 3*) is applied 1 inch lateral to the vertebral column, the lower one-third of which overlaps the upper one-third of No. 3, and runs in a similar course to No. 3, the end of which is attached temporarily to the skin below the right clavicle.

(3) To strap the right breast, the patient must be turned on the left side, the same procedure being carried out exactly as for the left, the difference being that the sternal ends of the strips of adhesive of the left breast are released, the patient turned directly on her back and made to adhere securely to the ends of the four strips from the right side, by overlapping them three or four inches (*Fig. 4*). Both breasts have been pulled medially, both being elevated to a point where the nipples are in the middle of each breast. Sterile gauze has been placed under the overlapping ends of the adhesive strips, and between the breasts, should they touch in the midline. The gauze frequently extends almost to surround or cover the nipple; this should be trimmed away to allow more than the areola to be exposed, or approximately 2 to 3 inches of each breast. To avoid raveling of the gauze, and to make the opening secure, small strips of adhesive about 3 inches long are used to seal the edges of the opening for each breast. Five or six of these short pieces are needed for each side. The nipples are protected by small sterile gauze pads (*Fig. 4*), secured by a strip of adhesive which extends from below the breast over to the top of the breast support. A shoulder strap of adhesive on each side is placed to keep the support elevated. It will be noticed that the adhesive tape is not applied directly to the skin of the breasts in any area.

This type of breast support may be worn for 5 or 6 days and then changed if necessary.

This method approaches the ideal (*Figs. 3, 4*) in the support of breasts for the following reasons:

(1) Painful breasts are relieved instantly (the patient will tell you so).

(2) Support is maintained uniformly without compression, either local or general.

(3) Expansion of the filling breast is permitted in all directions, thereby preventing blocking of the circulations, which allows the natural flow, barring previous obstruction of some of the channels.

(4) Milk will actually flow out of all areas of the breast. This relieves tension and engorgement, washes out infecting organisms, keeps the ducts open, prevents curdling of the milk, and preserves the milk supply.

(5) Engorged and caked areas can be prevented, and can be relieved by early application of this method.

(6) Blood circulation is preserved to the entire breast and nipple and infections are therefore unlikely to occur, high tissue resistance being maintained.

(7) Resolution is more prompt and more complete in inflamed areas. Development of and spreading of infections is therefore less likely.

(8) Nursing and care of the nipples are greatly facilitated. (This is appreciated most when the breasts are painful.)

(9) Protection to nipples and breasts is afforded.

(10) Irritation or rash from adhesive tape on the breast proper is avoided.

This type of breast support has been most successful in my practice. I have had only one case of cracked nipple, this in a very large breast, and have had not a single abscess in any of the cases thus far treated. I have attempted a more practical application of the idea of proper breast support by the invention of a new type of brassiere, the principles of which are based on the method of ideal breast support described (*Figs. 3, 4*) above. This brassiere (*Figs. 5, 6, 7*) indeed fulfills all the above requirements of the ideal method of supporting breasts, and does even more, namely:

(11) The entire brassiere can be removed with ease, as often as necessary.

(12) The nipples can be further protected

and kept clean by the application of a sterile nipple pad as often as is necessary.

(13) Flat and depressed nipples are frequently corrected without manipulation.

(14) Should an infection about the nipple develop, it can be treated easily without disturbing the breast proper.

(5) Should surgical procedure be necessary on one breast, postoperative treatment can be carried out with the greatest simplicity since this type of brassiere allows easy and complete exposure of one entire breast and at the same time maintains support to the other breast.

(16) Sagging of breasts may be prevented by use of the new type brassiere.

(17) To obtain the results advocated, every patient must be considered as individual and fitted as such.

CONCLUSIONS

(1) Only by a thorough and complete understanding of how and when infections of breasts develop can one hope to be successful in prophylaxis.

(2) An ideal physiologic method of breast support is demonstrated, based upon a comprehensive anatomical and physiological study of the gland.

(3) A more practical method of breast support is demonstrated in the new type brassiere (devised by the author), which not only fulfills all the requirements of the ideal method of support, but also greatly facilitates the management of pathological conditions.

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ANTERIOR PITUITARY GONADOTROPIC AND ANTERIOR PITUITARY-LIKE HORMONES IN THE TREATMENT OF CRYPTORCHIDISM*

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The efficacy of hormone therapy of non-descent of the testes and other anomalies of the male genital system by injections of anterior pituitary gonadotropic and anterior pituitary-like fractions obtained from pregnancy urine and from the placenta has recently been demonstrated by a number of investigators. There has been great variance in the results published and some controversy as to the wisdom of the treatment. Bevan[1] advocates surgical intervention before the advent of puberty, though more recently[25] concludes that the use of gonadotropic extracts is warranted as an experiment. Drake[2] believes that maldescent corrects itself spontaneously at or before the age of puberty and is of the opinion that the condition is not a surgical problem. Engle[3] and others advocate the use of anterior pituitary-like hormones, having as a basis the observed descent of the testes in immature monkeys following the injection of an extract of the pars anterior.

The total number of recorded cases is comparatively few. In the present report, a brief summary of these cases is presented and an account of 26 additional cases which I have personally observed during the past five and one-half years. It is hoped that these additional case reports may aid in the formation of more acceptable conclusions relative to the merit of hormone therapy.

SUMMARY OF REPORTED CASES

A summary of the results published by other observers up to December, 1937, is presented in *Table 1.* No attempt has been made to differentiate the various types of cases treated. Considering the group as a whole, it will be noted that of the 320 patients treated, successful results were achieved in 193, or 60.3 per cent. This series, though small, is sufficient to justify

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Table 1

SUMMARY OF REPORTED CASES OF CRYPTORCHIDISM TREATED WITH ANTERIOR PITUITARY-LIKE HORMONES*

Author	No. of Cases	Per Cent Descent		
		Complete	Partial	Failure
Aberle and Jenkins[4]	4	50	0	50
Brosius[5]	10	70	20	10
Cohn[6]	6	83	0	17
Cramer[7]	20	65	20	15
Dorff[8]	19	94	0	6
Farmer[9]	32	50	0	50
Goldman and Stern[10]	2	50	0	50
Hess and Kuhnstadter[11]	39	72	10	18
Huberman and Isrealoff[12]	6	50	50	0
Kuhnstadter[13]	13	77	0	23
Kuhnstadter and Robins[14]	3	100	0	0
McLellan[15]	25	56	12	32
Mimpriss[16]	20	30	0	14
Molitch[17]	11	64	0	36
Priestley and Cohn[18]	2	0	50	50
Roney[19]	6	57	0	33
Rubinstein[20]	8	37	25	37
Sexton[21]	18	55	11	33
Schapiro[22]	13	77	23	0
Sippe[23]	1	100	0	0
Spence and Scowen[24]	33	57	12	30
Thompson, et al.[25]	18	22	5	72
Webster[26]	11	81	9	9
Total	320	60.3	9.4	30.3

*In some instances the authors did not tabulate their results in percentages; therefore, these interpretations may vary from their published reports.

the conclusion that endocrine therapy is successful in at least one-half of the cases.

PRESENT SERIES

This study comprises a group of 26 patients, with one or both testes undescended, who have been treated over the past five and one-half years with anterior pituitary gonadotropic and anterior pituitary-like hormones. The preparations used in the early part of this study consisted of the anterior pituitary-like hormone from pregnancy urine (antuitrin-S,* Parke-Davis; antophysin, Winthrop; follutein, Squibb) or placenta (A.P.L.,* Ayerst-McKenna). Later, the anterior pituitary gonadotropic preparations (antuitrin gonadotropic,* Parke-Davis; maturity factor,* Ayerst-McKenna; prephysin, Chappell) were also tried. The pituitary hormones appeared to have no advantage over the pregnancy urine or placental preparations. The dosage varied with the individual case, but in the large majority of patients, 100 to 250 rat units were administered two or three times weekly, although daily administrations were given in some instances. The total amount administered ranged from 2,100 to 58,400 rat units over a period of from six to sixty weeks. The average period of observation was twenty-five weeks. The age at which treatment was begun ranged from 14 months to 29 years, but the greatest number were in the pre-pubertal period. None of the patients, with the exception of one who had been the subject of an unsuccessful operation, had received previous treatment. The cases were not selected, but were treated in the sequence in which they came to my attention.

Table 2 summarizes the original condition and the results in each case.

It may be seen that of the 26 patients, complete descent occurred in 14 (53.9 per cent), partial descent in 4 (15.3 per cent), and failure of descent in 8 (30.8 per cent). When classified according to whether the condition was unilateral or bilateral, the following values are obtained: unilateral (10 cases), complete descent 5 (50 per cent), partial descent 1 (10 per cent), and failure of descent 4 (40 per cent); bilateral (16 cases), complete descent 9 (56.2 per cent), partial descent 3 (18.8 per cent), and failure of descent 4 (25 per cent). Of the 12 cases in which incomplete or no descent was observed, orchidopexy was done in 2, with good results, and surgery advised in 1. In the remaining 9, further treatment has been abandoned either for lack of cooperation or failure of improvement after therapy.

A resumé of the more interesting features of some of the patients may now be considered.

Case 4.—Aged 9 years, was a poorly developed, undernourished child whom I have classified as hypoplastic and is considered here as evidence of the value of pre- and postoperative treatment (*Fig. 1*). The penis was almost completely surrounded by the scrotal fold, and the testes were not palpable in any position. The scrotum and penis were underdeveloped. He was given 8,800 rat units over a period of twenty-two weeks, at the end of which time the left testicle had descended and the right was palpable in the canal. Both, however, were rather small, but in keeping with the size of the penis. An additional 4,800 rat units during the next twelve weeks gave no further improvement. Orchidopexy was done and a band of fascia was found which prevented descent. When next seen, four weeks later, the left testicle had retracted into the canal, but the right, which had been surgically fixed, remained in the same position. Over a period of six weeks, 13,500 rat units were administered with remarkable success. The testes descended more completely, increased in size, and there was further development of the scrotum and penis.

*These preparations were generously supplied by the respective manufacturers. APL as used in this paper denotes any of the above anteriorpituitary-like preparations.

Table 2

SUMMARY OF CASES STUDIED IN THE PRESENT SERIES

Case No.	Age, Years	Constitution		Position		Treatment		Descent			Remarks
		Normal	Endocrine	Unilateral	Bilateral	Total Dose (Rat Units)	Duration of Treatment	Complete	Partial	Failure	
1	11		APG	R		5,200	13 weeks	X			Right could be pushed into scrotum before treatment
2	10		APG		X	19,200	60 weeks	X			Both descended at 16 weeks, but small. Remarkable development of genitals at 40 weeks
3	12	Frail		R		10,000	19 weeks	X			Descent at 12 weeks, but transient retraction. Permanent at 19 weeks
4	10	Hypoplastic			X	27,100	40 weeks	L	R		Left descended and right in canal at 34 weeks, both small. Right orchidopexy followed by APL; marked improvement
5	9		Thyro-pit.	R		28,000	56 weeks		X		Hernia developed on right. Small testis palpable in sac
6	1½	X			X	2,100	7 weeks	X			Treated at request of parents
7	10	X			X	58,400	56 weeks			X	Moderate increase in size of penis and scrotum and pubic hair. Testes not palpable
8	9	Hypoplastic			X	2,700	6 weeks		X		Making definite progress when treatment was discontinued
9	24		Hypogonad		X	11,550	21weeks			X	No objective or subjective effects from treatment
10	14	X		R		7,000	14 weeks			X	Right orchidopexy after 14 weeks' treatment; testis fixed in upper scrotum. Should continue treatment postoperatively
11	12	Hypoplastic			X	10,400	26 weeks	X			Complete descent
12	11		APG	L		23,000	44 weeks			X	Right normal before treatment. Left enlarged, but no descent
13	8	X			X	4,000	17 weeks	X			Complete descent in 6 weeks. Treatment continued to fix position
14	12		APG		X	29,500	49 weeks	X			Improvement more rapid after increasing medication
15	12		APG	L		56,000	36 weeks			X	Left enlarged, but no descent. Surgery advised
16	3	X			X	4,000	10 weeks	X			Complete descent
17	9		APG	R		8,000	20 weeks	X			Complete descent
18	12		Hypo-AP		X	6,075	9 weeks			X	Further treatment refused, though some progress
19	11/6	Extrophy of bladder and epispadius			X	3,800	10 weeks	X			Thought a female by parents. Complete descent and extrophy almost closed by treatment
20	17	X		R		4,050	9 weeks			X	No improvement. Orchidopexy with good results
21	9	Frail Pyknoleptic		R		9,600	24 weeks	X			Complete descent
22	12	X			X	24,000	24 weeks		X		Left descended to normal position Hernia with small testis on right
23	9		APG	R		21,000	7 weeks	X			Seen following failure of surgery; testis small and retracted. Marked improvement after "APL"
24	9		APG		X	10,670	39 weeks	X			Apparent precocious puberty 20 months after discontinuance of treatment
25	29		Hypogonad		X	19 200	32 weeks			X	No improvement
26	11	X			X	4,500	9 weeks	X			Complete descent
Total		14	12	10	16			14	4	8	

Fig. 1, Case 4

Aged 10 years. Bilateral undescended testes. A, before treatment. B, after 13,600 R. U. of APL aad surgical fixation of right testicle. C, following additional administration of 13,500 R. U.

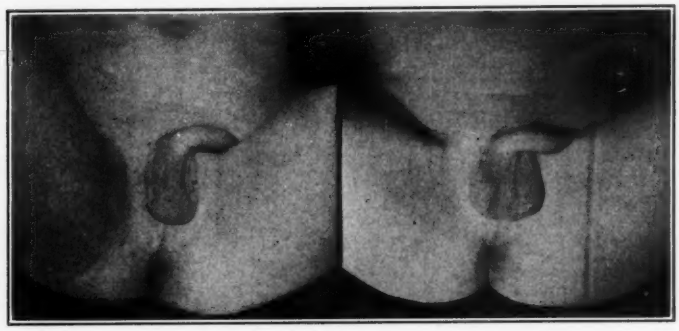

Fig. 2, Case 13

Before and six weeks after administration of 2,400 R. U. of APL.

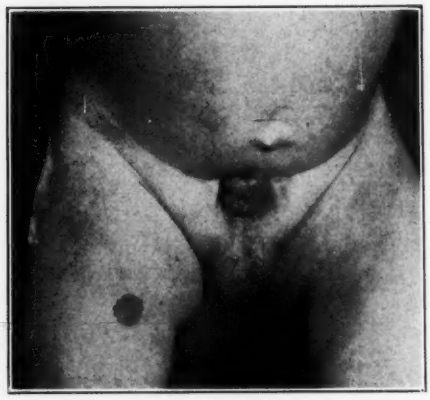

Fig. 3, Case 19

Aged 14 months (see text). Note almost complete closure of the extrophy, descent of testes, and increased size of the scrotum following APL therapy.

Case 13 (*Fig. 2*).—Aged 8 years, was a normal and well-developed boy. Both testes were of normal size and in the canals and could be manipulated to the upper pole of the scrotum. Treatment consisted of 4,600 rat units over a period of seventeen weeks. Complete descent occurred at the end of the sixth week (2,400 rat units), but treatment was continued to fix position. This case illustrates the type in which spontaneous descent might have occurred in later years, but also suggests the impracticability of waiting when descent can be hastened in some cases with APL therapy.

Case 19.—Fourteen months old. This unusual case presented some interesting features and demonstrates the value of endocrine therapy in the treatment of genital anomalies other than those commonly associated with cryptorchidism. The child was seen at the Crippled Children's Hospital, and treatment was instituted before I was consulted. On examination, a rather severe extrophy of the bladder, epispadius, bilateral non-descent of the testicles, and lack of development of the scrotum were found. The parents believed the child to be a female and had named her "Edna." After the administration of 3,800 rat units over a period of ten weeks, almost complete closure of the extrophy occurred, marked development of the scrotum, and descent of the testes (*Fig. 3*). The parents were greatly distressed by the revelation, and further treatment, medical or surgical, was refused in spite of the brilliant results accomplished.

Case 22.—Aged 12 years. This case is of interest because it brings up the question as to whether massive doses of the gonadotropic hormones bring about relaxation of the inguinal rings with the production of hernia. The boy's height, weight, and body build were normal. The left testis was palpable in the lower canal; the right was not palpable. After the administration of 2,400 rat units over a period of twelve weeks, the left testicle descended to normal position and a small right testicle was palpable high up in the canal. Therapy was continued until a total dose of 24,000 rat units was given in twenty-four weeks. At the end of this period a hernial sac appeared and a medium sized gland could be palpated (*Fig. 4*). Herniorrhaphy was done and the right testicle fixed in the upper part of the scrotum. Treatment will be continued in an attempt to assure complete descent of this testicle.

Case 24.—Nine years old and diagnosed as dystrophia adiposogenitalis, this case is described here because the end result suggests precocious development of sex characteristics. The penis and scrotum were small and atrophic; both testes were intra-abdominal. Complete descent of both testes and normal development of the genitalia were brought about by 10,670 rat units over

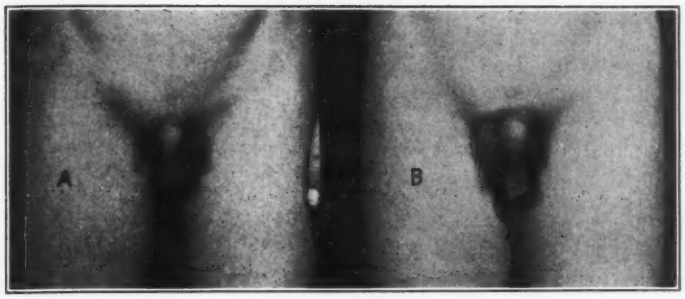

Fig. 4, Case 22

Aged 12 years. Descent of left testicle and appearance of a right hernial sac after a total dose of 24,000 R. U. over a period of twenty-four weeks.

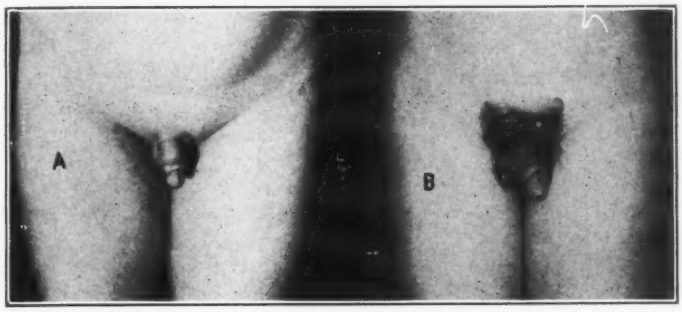

Fig. 5, Case 24

A, before treatment at age 9 years. B, twenty months after treatment with 10,670 R. U. Age 11½ years. Precocious sexual development is suggested by the pubescent hairs and enlarged genitalia.

a period of thirty-nine weeks. However, twenty months after treatment, when the patient was 11½ years old, an examination of the genitalia revealed advanced development for a boy of this age (*Fig. 5*).

DISCUSSION

A discussion of the literature has been omitted, because there have been so many clinical papers written on this form of treatment, and each paper has recapitulated all the preceding ones. Another recapitulation would be a work of supererogation. The satisfactory results obtained with endocrine therapy in 53.9 per cent of 26 patients in my series agree well with the reports of others. There appears to be no hard and fast rule, however, as to which type of case will respond more successfully, although such classifications have been attempted.[19 27] Of the 14 patients with a normal constitution, success was achieved in 8, and of the 10 with endocrine disturbances, 6 responded satisfactorily, or 57 and 60 per cent, respectively. These results are not in agreement with Rony, who is of the opinion that hormonal treatment is hardly necessary or successful in patients with no sign of disturbance in the endocrine system. Thompson,[28] Sexton[21] and others report marked effects in adults. In two of my patients (Cases 9 and 25) classical types of non-obese and obese hypogonadism, respectively, there were no subjective or objective signs of improvement despite prolonged treatment. These patients are receiving male sex hormonal therapy, with striking progress, and will form the basis of a future report.

In regard to dosage and length of treatment, about 500 rat units were administered weekly for 12 to 16 weeks. If any improvement was evident, therapy was continued for a reasonable length of time (up to 60 weeks in one instance) until the desired results were obtained. Occasionally descent occurred in 6 weeks if the testes were fairly well developed and in the lower end of the canal. It has been my experience that patients with palpable testes that do not enlarge or migrate perceptibly during the first 8 to 12 weeks of treatment probably will not respond to further therapy, although it is permissible to increase the dosage and continue the hormonal administration for another 6 to 10 weeks. If no response is evident at the end of this period, I believe further treatment is unwarranted.

I have found no correlation to exist between the dose of the hormone and the response. In *Case 1,* 5,200 rat units were sufficient to bring about complete descent, while in *Case 2,* 19,200 rat units were necessary for a similar result. In those cases in which descent occurred the earliest observed migration was 6 weeks, the latest 20 weeks. The penis and scrotum developed to normal for the age in most patients, and in the older boys pubic hair appeared.

Contrary to the reports of some authors, I have seen obvious inferiority mechanisms and other psychic disturbances associated with cryptorchidism and other genital anomalies. This psychological condition was corrected as the physical appearance improved.

The age at which treatment should be begun is highly debatable. Inasmuch as the scrotum is the normal position for the testis, it is logical to presume that the earlier the testis is placed in this position, the more normal will be its development. The retained testis is apparently not physiologically active, and frequently predisposes to other pathologic conditions in this region. I believe treatment should be instituted before the age of 8 years, and apparently there is no objection to beginning earlier. In 2 of my patients, therapy was started at the ages of 14 and 18 months (*Cases 6* and *19*) with no harmful effects.

Constitutional reactions were rarely observed and then only in the first few cases. Improvement in the products has practically eliminated these by-effects. In sensitive patients, the addition of 3 or 4 minims of solution of epinephrine served as a valuable adjunct in reducing anaphylactoid reactions to a minimum. No harmful effects were seen in any of the patients, with the possible exception of *Case 24*, which appeared to have accelerated secondary sex characteristics. In another patient (not included in *Table 2*), softening of the testes occurred during an attempt to develop an infantile penis with massive dosage after testicular descent was accomplished. This patient is now on androgenic treatment and will be reported in detail later.

It may be seen that one group of patients responded completely to treatment, with testicular descent and genital growth, while in another group testicular descent but no genital growth occurred, and in a third group no effect was evident. The exact mechanism of the action of the anterior pituitary-like hormone on sexual development remains unknown. APL preparations do stimulate the interstitial tissue of testes, inducing a liberation of the male hormone, which in turn stimulates development of the secondary sex structures.[29] In this manner, the complete response with descent and genital growth of the first group of individuals might be explained. The failure of the APL preparations in the remaining individuals presents a more difficult problem. Anatomical and structural anomalies must be considered. Failure might also be due to improper function of associated glands. It is well known that the efficacy of APL action depends on the presence of the pituitary. Furthermore, gonad development is also probably dependent upon proper functioning of the adrenal and thyroid. Careful consideration of all the embryonic and anatomic factors, as well as the different quantitative relations from the standpoint of the hormone involved, will help toward a better understanding of the problem.

CONCLUSIONS

(1) Twenty-six patients with cryptorchidism have been treated with anterior pituitary-like hormone. Descent of the testes has been obtained in 14 (53.9 per cent), partial success in 8 (30.8 per cent), and failure of descent in 4 (15.3 per cent).

(2) The average length of time of treatment was 25 weeks, with a total dosage of 13,000 rat units, corresponding to about 500 units weekly.

(3) In general, no serious complications have been observed, although in one patient precocious sexual development and, in another, softening of the testicle have been suggested.

(4) Endocrine therapy is of definite value as a preliminary to and following orchidopexy. The increased size of the testicle and lengthening of the cord elements permit better surgery, and the postoperative results are greatly improved by the treatment.

(5) Endocrine therapy should be given sufficient trial in perhaps every case of undescended testes and instituted preferably before the eighth year. The treatment is simple, without apparent harm, and with definite benefit to the majority of patients.

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SULFANILAMIDE IN THE TREATMENT OF GENITO-URINARY INFECTIONS*

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Approximately six months ago the drug sulfanilamide was advanced as a remedy useful in the treatment of various infectious conditions of the genito-urinary tract. In that period of time a rather extensive clinical trial has been given to the substance, making it possible now to evaluate to some extent its therapeutic usefulness and also its limitations.

The reception given to every new discovery in the field of medicine has been ingeniously reduced to a graph by Edwin Davis, who points out that new medications and procedures of definite worth invariably follow a set path of acceptance in the minds of the medical profession. This course of evaluation begins with general indifference, which presently gives place to overenthusiastic approval, sometimes commercially inspired by drug houses selling the preparation, or fostered by newspaper publicity; next, accidents occur, and pessimism supervenes, until finally, after a seesaw between hopes and fears, an awakening to the true therapeutic value of the drug or preparation arrives, and the product reaches stability at its proper level of usefulness. Sulfanilamide is running true to this form.

Following the work of the German chemists, Mietzsch and Klarer, on azo compounds, which resulted in the discovery of substances with far greater action on bacteria than any azo compounds previously measured, Domagk[1] observed an interesting activity on the part of certain of these compounds containing sulfonamide in the streptococcic sepsis of mice. Next came the discovery that the azo radical could be eliminated without impairing the antistreptococcic action. From this as a starting point came "prontylin," which is para-aminobenzene sulfonamide, first used therapeutically in Germany under the name of "streptozon" and later as sulfanilamide. Curiously enough, the new compound displayed almost no disinfectant action *in vitro* and it had no effect of any kind upon healthy mice, but its

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action upon certain strains of streptococci seemed specific. Against the staphylococcus also it was strongly bactericidal, while the effect upon the pneumococcus was to inhibit its growth.

The first American report was made by Long and Bliss[2] early in 1937, on the basis of 70 cases treated, with 4 deaths, only one of which, however, could fairly be attributed to failure of the treatment. Shortly afterwards, Helmholz reported that the urine of patients to whom sulfanilamide has been administered develops definite bactericidal properties against such organisms as commonly flourish within the urinary tract. Among these, he found the staphylococcus to be the most easily affected, while at the other end of the range stands *Streptococcus fecalis,* which continues to grow luxuriantly in urine that will completely inhibit the growth of the gram-negative group in twenty-four hours. He also observed that the new drug is more effective in alkaline than in acid urine, and that the urine tends to be alkaline after its administration. He expressed the view that its ease of administration, its action in alkaline urine and its successful use in clearing up infections resistant to mandelic acid made it a urinary antiseptic of great value.

Then Dees and Colston,[3] working at Johns Hopkins University Hospital, recorded that sulfanilamide has a definite bactericidal effect on the gonococcus. Since it is difficult to infect animals with this organism, they tried the clinical application of the new drug in 19 cases of gonococcal infection, finding that in nearly all instances the discharge disappeared within 1 to 4 days after treatment was instituted, and most of the smears were negative for gonococci in 2 to 5 days.

Because these authorities have been widely quoted we wish to emphasize at this time that while negative smears may be obtained in 2 to 5 days it does not mean that the infection has been eliminated. In numerous instances where a short course of the drug is given the organism will again be found in the urethra within 10 to 12 days after the medication is stopped. Careful observation and frequent tests of cure are important when sulfanilamide is used in treating gonorrhea.

Dees and Colston were also impressed with the fact that the infection had not extended from the anterior to the posterior urethra, thereby minimizing possible complicating factors, and in this we heartily concur. Since February, 1937, we have been using sulfanilamide at our clinic in genito-urinary infections of the most varied kind, and it is our opinion that its therapeutic value in these conditions when properly administered is important.

NONSPECIFIC INFECTION OF THE URINARY TRACT

Pyelitis.—In our experience acute upper urinary tract infections respond quite satisfactorily to the medication, except in cases of stone or stasis, where of course the causative factor must be removed before infection can yield to treatment by chemotherapy. In other conditions we feel that the course of the infection is materially shortened clinically and the symptoms are ameliorated. This is evidenced by a more rapid fall in temperature and by clearing of the urine. Where sulfanilamide cannot be administered by mouth because of gastric intolerance, we have successfully given it in 0.8 per cent solution by hypodermoclysis. Acute bacillary infections of the kidney have responded more satisfactorily than the coccal infections.

Cystitis.—Administration of the drug in instances where bladder infections occur following surgical procedures on the bladder neck has not been particularly successful, especially in the first few postoperative weeks. When, however, sufficient time has elapsed for all necrotic material to be eliminated from the operative area, sulfanilamide is an aid in relieving the residual infection.

Acute trigonal cystitis, seen often in women, and usually of bacillary origin, is uniformly aided by the drug. Rarely will acute bladder symptoms persist more than twenty-four hours after its administration. Nevertheless, it is advisable to continue therapy until the offending organism has been completely eradicated.

Nonspecific Prostatitis.—Results obtained in nonspecific infection of the prostate where the gonococcus is not present have not been altogether satisfactory. Although administration of sulfanilamide will produce a decrease in the extent of the infection, revealed by microscopic examination of the expressed secretion, recurrences are frequent when the drug is discontinued. Neither persistence in the medication nor the size of the dose seems to alter the situation materially. Twenty to thirty grains of the drug will produce as much benefit as a more massive dosage. For the desired results more dependence must be placed on regular prostatic massage over a sufficient period of time.

In our experience the administration of sulfanilamide in small doses (30 grains daily) for a few days before operative procedures are performed on the urinary tract reduces the intensity

of possible postoperative reactions. In cystoscopic manipulation for ureteral calculi, fulguration of urethral conditions, or prostatic resections it is evident that the drug by inhibiting bacterial growth shortens the convalescent period.

GONOCOCCUS INFECTION

When one realizes that this medication is not specific for gonococcal infections it may be said that our results obtained in the treatment of gonorrhea have been quite satisfactory. Over 300 such patients have been treated with the preparation, the majority of these being in private practice. Sulfanilamide therapy in dispensary patients is accompanied by difficulties, because of an inability to observe the progress in these patients until a definite cure has been accomplished. Invariably this class of patients fails to return to the clinic when gross evidence of their infection disappears. A false sense of security is engendered in them through the erroneous belief that they have been cured and as a result they will return to normal sexual activities, thereby causing a wider spread of the disease. As a point in the public health control of gonorrhea we feel that this phase of sulfanilamide therapy has not been sufficiently emphasized.

In acute anterior urethritis of gonococcal origin we have found the drug most useful in preventing posterior complications and extension. It must be remembered, however, that the ultimate cure is brought about by the patient's own immunological response to the infecting organism. If the drug so inhibits the growth of the gonococcus that this immunological reaction is lessened or slowed down, the complete cure may be hindered instead of hastened. We must also bear in mind that by lessening the discharge sulfanilamide eliminates evidence of the disease, allowing the patients, and sometimes even the physicians, to think that a cure has been accomplished when this is not the case. In this way the possible spread of the disease may actually be encouraged.

DOSAGE OF SULFANILAMIDE

It has been our aim to keep the dosage of the drug within reasonable bounds. We do not share the view of Dees and Colston, of Long and Bliss and certain other authors that it is important to administer a large amount (80 grains) during the first twenty-four hours of treatment, and then lessen the dose by a third or a half on the third and fourth days. It has not been necessary to give more than 60 grains daily (divided into 4 doses) for 2 days; we cut this down to 40 grains for the next 5 days, and to 30 grains during the second week. If renal function is poor, and there is evidence of possible lack of tolerance, the initial dose is smaller than 60 grains. A dosage of 80 grains a day for 2 days, which was first advised for streptococcic infections, is in our opinion unnecessarily large for the average patient who is ambulant and attempting to work, and will invite complications.

Experience has shown that no standard dose can be established, since the amount must vary with the individual patient. In younger patients the kidneys will excrete the drug more rapidly, and will thus lessen the blood level of the drug. On the other hand, if the substance is excreted slowly by the kidneys, the blood level will be raised, even though the dosage of the drug is small. This possibility of impaired renal function must always be taken into consideration.

DETERMINATION OF BLOOD LEVEL

A simple method for the exact determination of the level of the drug in the blood and urine has been worked out by Marshall, Emerson and Cutting[4] at the Johns Hopkins University. The accuracy of the procedure has been carefully established and it is found that duplicate determinations check within 2 or 3 per cent. The human subject excretes the drug partly unchanged and partly in conjugated form. Because of the slower excretion when the kidney function is impaired, sulfanilamide should be given with very great care, always keeping in mind the possibility that the drug level in the blood may be higher than is safe. Buchtel and Cook state that in their experience the individual tolerances differ markedly, so that it is a most difficult drug for which to standardize the dosage. Marshall and his coworkers say of their method that it is possibly the best renal test ever developed. Probably such determinations will be done more frequently in the future in cases presenting intolerance to medication.

Some urologists, as Cook and Buchtel,[5] begin, not with large doses that are to be decreased, but in just the opposite way: Walther, for example, writes that he considers it much safer to begin with definitely small doses (18 grains daily) (1.2 gram) for two days, and then to increase these if they are well tolerated. Beginning then with the fourth day, he gradually increases the amount until he reaches 80 grains daily.

Rarely is the drug given for more than two weeks, for it is found that the optimal results are

obtained within this length of time. The first ten days is the golden period of therapeusis so far as sulfanilamide is concerned. Doubtless the offending organisms by that time have built a tolerance toward the medication that hinders a complete cure. Furthermore, we believe on general principles that continuous medication with one and the same preparation over long periods of time is fraught with danger, because of the possible cumulative effect. With sulfanilamide this danger would seem especially great, due to its possible depressing effect upon the hematopoietic system.

COMPLICATIONS

Serious complications encountered in our experience with the drug have been surprisingly few. We believe that our conservatism in dosage, together with frequent observation of the patient, contributes to this end. We are convinced that the drug is of such importance as a therapeutic agent and holds such potentiality for the development of serious complications if carelessly administered, that no patient should be entrusted with it for any length of time without close medical observation. No need has been felt for daily blood counts to determine whether anemia is present, since the general appearance and state of well being of the patient have in all cases given a sufficient hint as to his tolerance. Whenever any undue difficulty is encountered, cessation of medication has uniformly resulted in rapid improvement. As an added safeguard, the drug is dispensed from the office only in such quantities that no more than two or three days' supply is held by the patient.

Among specific complications met with, skin manifestations have constituted the majority. In the few dermatoses that have been produced, it has been possible to discontinue the drug for a few days and return to it at a later date when the eruption has disappeared; and in no cases has there been a recurrence, although this has been frequently reported by other writers. Practically all the patients complain of dizziness and lassitude, together with loss of appetite. Unless these symptoms are unusually severe, they are ignored, as we feel they indicate satisfactory systemic absorption. By the second week these manifestations usually diminish in intensity. In this series no serious instances of anemia have developed, as some authors have reported. One patient developed an optic neuritis while under treatment, which may have been due to the drug. Fortunately this condition improved upon withdrawal of the drug.

Sulfhemoglobinemia and methemoglobinemia, against which a number of authors have uttered a warning, have not been observed among our patients. Caution is observed that no magnesium sulphate or other saline cathartics are taken with the sulfanilamide, nor do we allow any other adjuvant medication except sodium bicarbonate.

Before leaving the subject of complications, it seems that reference should be made to the very recent reports of 73 deaths from the use of a so-called "elixir of sulfanilamide" that has been sold without its producers having tested its properties. Investigation has brought to light the fact that these deaths were probably due to the presence of large amounts of diethylene glycol, and not to the sulfanilamide ingredient. The chief symptom in these fatal cases was anuria, which has never been observed following the ingestion of sulfanilamide, but which has now been shown by animal experimentation in the laboratories of the American Medical Association to follow the use of diethylene glycol. The latter substance is not a pharmaceutical remedy, but a toxic preparation used in the mechanical arts, entirely unsuitable for human consumption.

RESULTS IN TREATMENT OF GONORRHEA

An evaluation of the results obtained with this type of medication in gonorrhea is still somewhat difficult. We feel that the benefit accruing from shortening the length of time of active symptoms and the lessened number of complications as compared with that of the past has proven the drug to be a very valuable adjunct in treatment of gonorrhea. In our hands, however, it has not replaced the more accepted methods of treatment for this disease.

As the cure of gonorrhea is based on a personally developed immunologic reaction between host and organism, and as stimulating local therapy in conjunction with proper hygienic control of the patient is a potent factor in promoting this immunity, we have been loth to dispense with these time-honored methods of treatment. For these reasons, patients are given the same therapeutic routine as formerly, and sufficient time of observation is taken before they are discharged as cured.

Briefly, our records show: ten per cent of the patients with an acute anterior gonococcal urethritis treated with sulfanilamide will apparently be radically cured within forty-eight hours. By a radical cure we mean that continuous observation of these individuals over a period of weeks

combined with repeated "tests of cure" produced no evidence of the disease. Seventy-five per cent of patients will be improved by administration of the drug as shown by diminution in the amount of urethral discharge, with recovery completed at the end of four to six weeks. Fifteen per cent of patients seem to obtain no therapeutic results whatever with the medication. They continue to have signs and symptoms of infection for long periods of time, with or without complications in the form of acute and chronic prostatitis. However, serious complications have been markedly reduced and those that do occur may be explained as due to a lack of normal resistance to the disease or on a basis of poor behavior. The acute symptoms of posterior urethritis are rapidly relieved by the drug. The benefit from sulfanilamide in acute epididymitis has been less spectacular. It apparently does not materially shorten the course or intensity of this complication. In our experience, acute iridocyclitis and arthritis have also been disappointing in response to this treatment.

The results in chronic gonococcal infections, occurring in those who have not received the drug previously, have been extremely satisfactory. Chronic prostatitis of gonococcal origin is apparently rapidly improved by the medication, as determined by examination of the expressed prostatic secretion and appearance of the urine. If, however, nonspecific infection be present as a complicating factor, the end results are not satisfactory. As these nonspecific infections of the prostate gland constitute a large proportion of the infectious pathologic conditions of this gland, and as it is practically impossible to differentiate these from gonococcal infections, the difficulty is obvious in evaluating this phase of therapeutic benefit.

Peri-urethral infection of gonococcal origin has been less favorably influenced by the drug than prostatitis. In such cases we find that infection tends to persist, and more dependence must be placed on local measures. Possibly the concentration of the drug when it is excreted in the prostate gland is much higher than that which obtains in the glandular structure of the anterior urethra.

In conclusion, sulfanilamide is a valuable therapeutic measure for use in genito-urinary infections. When it is properly employed, with strict attention to its capacity for producing harm and a clear knowledge of its limitations, it is a worthy addition to our medicinal armamentarium. At times the results produced in combating gonorrhea are spectacular, but it frequently masks the signs and symptoms without eradicating the infection completely. Provided the physician is aware of this fact, it will prove to be a drug of tremendous merit in diminishing the clinical intensity of the disease.

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Discussion follows paper of Drs. Alyea, Daniel and Harris, page 405.

SULFANILAMIDE IN THE TREATMENT OF GONOCOCCIC INFECTIONS IN THE MALE*

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The results obtained by the use of sulfanilamide in gonococcic infections were first reported in American literature by Dees and Colston.[1] There have been numerous reports of experimental and clinical observations regarding the use of the drug in various infections. Long and Bliss[2] reported its use in *beta* hemolytic streptococcal and pneumococcal infections, as well as the mode of action and toxic effects. Cook and Buchtel[3] have reported 200 cases of urinary tract infections treated with sulfanilamide. Marshall, Emerson and Cutting[4] reported a method for determining the sulfanilamide content of body fluids.

It is my purpose to present to you the results obtained in a series of 148 cases of gonococcic infection in the male treated with sulfanilamide

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and "prontosil." All of the common types of gonococcic infections in the male have been encountered in this series. These were private patients treated by my associate, Dr. F. L. Van Alstine, or myself, and in most instances they have been more cooperative than those seen in the average clinic. I have not included patients who came to the office only a few times. All were ambulatory except one who was hospitalized.

The majority of the patients with acute infections received 20 grains of sulfanilamide, orally, four times a day for the first two days; 15 grains four times a day for the next three days; 10 grains four times a day for the next seven days; and thereafter, 10 grains three times a day until the drug was discontinued. Many of the chronic cases did not receive more than 60 grains daily at any time. All were advised to take 20 grains of bicarbonate of soda three times daily, to avoid the use of any laxative which would produce a liquid stool, and to report any untoward symptoms. The drug was not given to patients unless they would agree to report to the office at frequent intervals for observation. When possible, the patients discontinued work during the time they were taking the large dosage.

On account of the variation in tolerance of sulfanilamide, the dosage scheme was varied according to the reaction of the individual. Dosage was decreased on appearance of headache, marked dizziness, anorexia, or extreme cyanosis. The drug was discontinued at the first sign of fever, dermatitis, complete loss of appetite, or evidence of anemia. These patients were usually not given the drug again even in small doses. There have been numerous reactions, none serious, and all have cleared up on discontinuation of the drug and ingestion of large quantities of water.

Several of the patients received 10 c. c. of "prontosil" intramuscularly, daily or on alternate days, in addition to sulfanilamide. None was treated with "prontosil" alone, since it was felt this would require too many visits daily to the office. I could detect no definite benefit from "prontosil" in those patients who tolerated sulfanilamide well. "Prontosil" seemed to be beneficial to many of the patients who were unable to tolerate sulfanilamide or tolerate it only in small doses. It satisfied the type of patient who wanted "shots;" the red color imparted to the urine produced a good psychological effect, and many patients would return with more regularity for "shots" than for observation alone.

The diagnosis in each case was made on the demonstration of gram negative intracellular diplococci, having the morphological appearance of the gonococcus, in stained smear of urethral discharge, prostatic smear, or sediment from centrifugated urine. Cultural methods were not used.

For the purpose of this report, these patients have been divided clinically into three groups, depending on the condition present at the time of the first examination.

Group I, consisting of 78 patients, was classified as acute anterior urethritis. This diagnosis was based on the finding of cloudy first voided urine, clear second voided urine, and no evidence of infection in the prostate.

Group II, consisting of 39 patients, was classified as acute anterior and posterior urethritis, with complications. In this group, not only was the first and second voided urine cloudy, but some acute condition was present, such as prostatitis, epididymitis, seminal vesiculitis, arthritis or peri-urethral abscess.

Group III, consisting of 31 patients, was classified as chronic anterior and posterior urethritis, with complications. The infection in all of these patients was of more than one month duration; first and second urine was cloudy, but no acute symptoms were evident. Practically all of these had pus in the prostatic smear; several had urethral strictures; however, a few were nearly symptomless at the time treatment was instituted.

Each group has been subdivided into three classes, according to the response of the patient to sulfanilamide.

Class A.—These patients were able to take sulfanilamide without evidence of intolerance; there was good response to the drug, and the infection cleared up without any adjuvant treatment.

Class B.—These patients were able to take sulfanilamide at least in moderate or small dosage. The infection showed some response to the drug, but it was necessary to use some adjuvant treatment. Generally speaking, if at the end of ten days the patient still had urethral dis-

charge, or smear was still positive for gonococci, or the patient had some reaction making it necessary to temporarily discontinue the drug once treatment was started.

Class C.—This class consists of those patients who, on account of reactions, were unable to take sulfanilamide and those patients who were able to take the drug but whose infection showed little or no improvement. Some of the patients who had reactions were benefited during the time they were able to take the drug and it probably shortened the period of infection. Local treatment was necessary in each case.

The patients in Group I who responded best to sulfanilamide alone were those who reported early with only a slight urethral discharge and those who gave a history of having had a previous gonococcic infection. The majority of patients with a profuse urethral discharge obtained relief from burning on urination and decrease in redness about the meatus, although a slight discharge persisted and some local treatment seemed necessary. Only four patients in Class A had any complication and this consisted only of a transitory cloudiness of second urine. The majority of complications in Class B were mild and frequently lasted only a few days. There are two patients in Class C who are still under treatment for chronic prostatitis.

The majority of the patients in Group II with frequency, urgency, nocturia, pain, and burning, experienced almost immediate symptomatic relief. Second voided urine usually cleared rapidly, and in most cases, progress of the disease was apparently checked. In four of six cases of acute prostatitis there was a dramatic response to the drug. In eight patients with epididymitis, the swelling, pain, and tenderness decreased more rapidly than with any previous

GROUP I: ACUTE ANTERIOR URETHRITIS (78 CASES)

	Class A 23, or 29.5 per cent	CLASS B 37, or 47.5 per cent	CLASS C 18, or 23 per cent
Discharge stopped (average)	4 days	8 days	22 days
Negative smear (average)	9 days	22 days	46 days
Complications	4 patients	21, or 56.7 per cent	14, or 77 per cent
Considered cured (average)	20 days	39 days	74 days*
Time followed (average)	26 days	45 days	82 days
Recurrence of reinfection	4 patients	6 patients	3 patients
Previous infections	11 patients	14 patients	7 patients

*Two patients still under treatment after 120 days.

GROUP II: ACUTE ANTERIOR AND POSTERIOR URETHRITIS WITH COMPLICATIONS (39 CASES)

	CLASS A 17, or 43.6 per cent	CLASS B 12, or 30.8 per cent	CLASS C 10, or 25.6 per cent
Discharge stopped (average)	6 days	14 days	31 days
Negative smear (average)	18 days	29 days	44 days
Second voided urine clear (average)	4 days	10 days	23 days
Considered cured (average)	22 days	42 days	56 days*
Time followed (average)	35 days	53 days	78 days
Recurrence or reinfection	3 patients	4 patients	2 patients
Previous infections	5 patients	6 patients	4 patients

*Except three patients who required 84, 89, and 108 days.

GROUP III: CHRONIC ANTERIOR AND POSTERIOR URETHRITIS WITH COMPLICATIONS (31 CASES)

	CLASS A 16, or 51.6 per cent	CLASS B 9, or 29.1 per cent	CLASS C 6, or 19.3 per cent
Discharge stopped (average)	3 days	7 days	33 days
Second voided urine clear (average)	4 days	5 days	24 days
Negative smear (average)	14 days	17 days	61 days
Considered cured (average)	18 days	32 days*	76 days*
Time followed (average)	27 days	48 days	82 days
Recurrence	3 patients		1 patient
Previous infections	9 patients	7 patients	2 patients

*One patient in Class B and two in Class C have an occasional gram negative diplococcus after 120 days.

treatment. Four who have a mild residual prostatitis are symptom-free and repeated smears have failed to show gram negative diplococci. The infection was cleared up in 17, or 43.6 per cent, with sulfanilamide alone. The response in many patients of this group might be explained by the fact that gonococcic infections frequently clear up following some complication with fever, such as acute epididymitis.

In Group III, many of the patients were practically symptomless at the time treatment was started. Sixteen, or 51.6 per cent, of the patients in this group responded to sulfanilamide alone. Prostatic massage and the passage of sounds was necessary in many instances only as diagnostic procedure. Twelve of these patients are still under treatment for chronic prostatitis and one patient in Class B and two in Class C still have an occasional gram negative diplococcus in centrifugated urine after 120 days of treatment.

SUMMARY

Sulfanilamide is the most efficacious drug yet advocated for the treatment of gonococcic infections. While it will apparently cure within twenty to thirty-five days slightly more than one-third of the gonococcic infections commonly seen in the male, the dosage must be carefully regulated by a physician who realizes the dangers of the drug. Since local treatment has proven necessary in approximately two-thirds of the patients, I believe it advisable to use local measures in addition to sulfanilamide in all cases at the beginning of treatment.

There have been no serious toxic manifestations in this series. They have been carefully watched and at the first appearance of toxicity, the drug was either discontinued or the dosage reduced. The progress of the disease was checked in practically all patients who were able to take the drug and complications were greatly reduced. When complications occurred, they were usually less severe in patients who were taking sulfanilamide.

"Prontosil" solution, intramuscularly, seemed beneficial in that group who tolerated sulfanilamide only in small doses. I could detect no benefit from "prontosil" in patients who tolerated the maximum dosage of sulfanilamide. Patients receiving "prontosil" returned for treatment with more regularity, and the red color imparted to the urine produced a good psychological effect.

To summarize briefly my experience with the drug in the treatment of gonococcic infections in the male, approximately one-third were cured, one-third benefited, and one-third unable to take the drug or the drug was of little or no benefit to them.

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Discussion follows paper of Drs. Alyea, Daniel and Harris, page 405.

SULFANILAMIDE THERAPY IN GONORRHEA AND ITS COMPLICATIONS*

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Medical therapeutics is entering upon a new era in chemotherapy stimulated by the experimental and the clinical results obtained in the use of prontosil. This substance is broken up in the body and the active principle liberated is para-amino-benzene-sulfonamide or sulfanilamide as it is now called. To go into details of the history and progress of this drug would be unnecessary and unwarranted repetition. Long[15] and others have covered the subject thoroughly in recent literature. I wish only to mention a few of the pioneers among the experimental workers with this new compound.

Forester, in 1933, first reported the beneficial effect of the use of "prontosil" in a case of a generalized staphylococcic infection. A year later, Grutz used it in cases of septic erythema with most encouraging results. In 1935, Veil reported a series of cases with infectious arthritis, all of whom improved markedly on its use. It was after this that the first experimental work done by Domagk[10] in 1935 was reported. He protected mice infected with beta hemolytic streptococci by the use of "prontosil." In France, Levaditi[14] corroborated these results. A year later Colebrook,[7] in England, used the drug clinically in a series of cases with puerperal fever. The clinical results were as encouraging as the experimental. Subsequently many and various reports came from Germany, France and England of the clinical use of this drug in streptococcic infections. Buttle,[5] in the same year, experimented with the benzene sulfonamide radicals and found that the drug, para-amino-benzene-sulfonamide, was the active principle of "prontosil."

Long and Bliss introduced the drug in this country and reported their clinical work with sulfanilamide in the treatment of beta hemolytic streptococcic infections. They also suggested its use in meningococcic and gonococcic infections. It was in May, 1937, that Dees and Colston[8] reported the first series of cases of gonorrhea treated with sulfanilamide; in this series of 47 cases the results were remarkable. It was later found that Reuter[23] in Washington had been using it and had a series of 100 cases of gonococcic urethritis in which he had obtained similar results. Levaditi then published his experimental work with "prontosil" and the gonococcus. All his mice protected with sulfanilamide survived, while the unprotected mice died of gonococcic peritonitis. Long has verified this work.

Sulfanilamide is now being widely used clinically in the treatment of infections caused by the staphylococcus, streptococcus, gonococcus, meningococcus. Recently bacillary infections in the urinary tract have been cleared up rapidly with its administration. Its wide chemotherapeutic application is fast being recognized and we believe that not since the days of Ehrlich and arsphenamine has a new drug shown such promise.

Marshall[16 18] and others have discussed the physiology and pharmacology of sulfanilamide. Clinically we are particularly interested in its absorption and excretion. Sulfanilamide is absorbed quite readily into the blood stream where it is changed into the free or active form, and the conjugated or acetylated form which is inactive. We have determined the blood concentration of this drug one, three, and five hours after oral administration and find that the maximum concentration is reached in three to four hours. This can be determined from the plasma, serum, or the whole blood itself since the concentration is the same in all. Marshall has shown that the blood concentration of sulfanilamide is easily maintained between 1-5000 and 1-10,000. It has also been shown that sulfanilamide in human blood is bacteriocidal against streptococci at a concentration of 1-13,000 to 1-18,000, so that this is a drug which at an easily maintained level renders the blood bacteriocidal to beta hemolytic streptococci. It has also been demonstrated that oral administration of sulfanilamide is just as effective as subcutaneous injection.

Chart 1

BLOOD SULFANILAMIDE

Dosage:
6 gms. the first day
3 gms. each day following for two weeks
Fluids to 2,000 c. c.

Determination three hours after dose

Second Day:	Blood Sulfanilamide
Lowest	2 mg. per cent
Highest	22.5 mg. per cent (Impaired renal function)
Average	6.2 mg. per cent
Fifth Day:	
Lowest	2 mg. per cent
Highest	9 mg. per cent
Average	5.5 mg. per cent

Impaired renal function requires a much smaller dose to obtain same concentration.

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Several hundred blood concentration determinations of the free sulfanilamide convince us that the level depends upon many factors: the dosage administered, the fluid intake, absorption from the gastro-intestinal tract, the ability to conjugate the drug, and renal function. The average determination in this series made in patients on a dosage of 6 grams the first day and 3 grams each day after that, with a fluid intake level of 2,000 c. c. in 24 hours was 6.2 mg. per cent. The lowest level was 2 mg. per cent and the highest was 22.5 mg. per cent. The latter was in a case with impaired renal function; it is known that patients with damaged kidneys require a much smaller dose of the drug to obtain the desired blood level. In this series we checked the concentration on the second, third and seventh days and discovered that it remained at about a constant level. Ninety-five per cent of sulfanilamide is excreted through the kidneys in two forms: the free or active, and the conjugated or acetylated, the inactive form. Marshall has found that the dog excretes most of his sulfanilamide in the free form; while the rabbit, on the other hand, excretes most of it in the conjugated or inactive form. Many determinations on man's urine show the average proportion is 80 per cent in the free or active and 20 per cent in the conjugated form. However, some of the patients have excreted an equal quantity of both free and conjugated. It occurred to one of us that perhaps herein lay the solution of the question why some individuals are cured and others not benefited by treatment with it. This will be discussed later. The drug is quickly excreted in the urine. If fluids are forced to five or six thousand c. c., practically all of the drug is excreted in 24 hours.

The mode of action of this new drug forms a most interesting chapter.

Domagk and Long suggested that it stimulated the white cells to increased phagocytosis. Particular attention has been paid to this in examining urethral smears during the first two days of treatment. It is difficult to form an opinion on this, because in 12 to 24 hours after the initial large dose there are very few bacteria visible. Cooper, Bliss, Peebles, Weinberg, Mellon and Shinn have observed no increased phagocytosis. It has been suggested that perhaps the bacteria may be rendered more easily susceptible to phagocytosis. Gross, Cooper and Peebles believe that the possible role of the reticuloendothelial system is rendered unlikely by the fact that splenectomized animals are also protected with this drug. Levaditi and Vaisman suggested that sulfanilamide acted by preventing a capsule formation around the bacteria and thereby rendering them more vulnerable. Helmholz and Long have reported the bacteriostatic property of this drug in the urine. It is quite likely that it does work in this manner in urinary infections, but this would not explain its action in the systemic infections. Colebrook suggested that the patient's serum has a bacteriostatic action *in vitro* and that the infection with the organism was necessary for activation of the sulfanilamide against the organism. Recently Welch[28] has suggested that sulfanilamide has a direct action on certain bacteria preventing rapid multiplication and enabling the body defense mechanism to cope adequately with the organism. Long has shown that there is marked increase in phagocytosis in the peritoneal exudate of mice infected with gonococci. He also has shown that mice rendered granulocytopenic by treatment with benzene do not react favorably under sulfanilamide therapy. Hence his conclusion is that leukocytes are necessary for the beneficial effect of sulfanilamide. Most probably it works by rendering the bacteria more easily ingested or by increasing the phagocytic power of the white cells.

All of the blood concentrations of the free sulfanilamide were determined by one of us (J. H.) according to the method of Marshall.[17] We quote:

"To two c. c. of whole oxalated blood were added 14 c. c. of distilled water. After hemolysis was completed, 4 c. c. of 20 per cent para-toluene sulfonic acid solution (in water) were slowly added with shaking. After five minutes the mixture was filtered and to 10 c. c. of the clear filtrate was added 1 c. c. of a freshly prepared 0.1 per cent aqueous sodium nitrite solution. Three minutes later 5 c. c. of 0.4 per cent solution of dimethyl-a-naphthylamine in 95 per cent alcohol were added. The color developed at the end of 15 minutes was then compared with that of a standard treated in exactly the same manner as the blood filtrate. Since the color developed is not exactly proportional to the concentration of sulfanilamide, we have found it necessary to use at least three standard solutions. These contain 18 c. c. of the 20 per cent paratoluenesulfonic acid solution and 0.25, 0.50 or 1.0 mg. sulfanilamide per 100 c. c."

All of the bloods were examined with a pocket spectroscope to determine the presence of sulfhemoglobin or methemoglobin bands in the red region. If the band persisted after the addition of cyanide, the presence of sulfhemoglobin was established. Methemoglobin bands in the red region of the spectrum disappeared after the addition of cyanide. Quantitative determination of these pigments were performed by a spectrophotometric method of Michel which is soon to be published.

The correct dosage to be used in the treatment of gonococcic infections is still uncertain. Long has suggested a large dose the first day with one-half the size dose the following days over a period of ten days or two weeks. In following his suggestion we began with 6 grams the first day and 3 grams a day for the following thirteen days. With this dosage our aver-

Chart 2

DOSAGE

Long:
6 gms. first day
½ dosage succeeding days

Dees and Colston:
4.8 gms. for two days
3.6 gms. for three days
2.5 gms. for four to eight days

Buchtel and Cook:
4.5 gms. for one to two days
2.6 gms. for ten days
1.3 gms. for two weeks after U. D. stopped

Orr:
4.8 gms. for four days
2.4 gms. for four days
1.2 gms. for seven days

Author's:
6 gms. first day
3 gms. each following day for two weeks

age blood concentration level of sulfanilamide was between 6 and 7 mg. per cent. Reuter, in his series of 100 cases with excellent results, used only 4 grams daily. Orr[21] used 4.8 grams for four days, 2.4 grams for four days, and 1.2 grams for 7 days. Buchtel and Cook,[3] and Colston and Dees suggested practically the same dosage. None of these men reported the control of the fluid intake or blood concentrations. Inasmuch as the blood concentration may vary with the fluid intake all of our patients were given 2,000 c. c. daily.

In this series of 158 cases there are, as shown in *Chart 3,* 65 of acute gonococcal urethritis, 30 chronic gonococcal urethritis and prostatitis, 6 acute epididymitis, 4 acute gonococcal prostatitis, 10 acute gonococcal trigonitis and posterior urethritis, 5 gonococcal infections of a paraurethral duct or gland, and 6 cases of acute gonococcal arthritis. These patients were followed carefully until their cure. Some were seen several weeks or months after their treatment was stopped. In addition to this group there were 32 patients who were treated, but were not seen again and have not answered our questionnaire. While it may be fair to judge that "no news is good news," they have not been included in this report.

Chart 3

	Cases
Acute G. C. urethritis	65
Chronic G. C. urethritis and prostatitis	30
Acute epididymitis, G. C.	6
Acute prostatitis, G. C.	4
Acute trigonitis, G. C.	10
Infection of paraurethral duct or gland	5
Acute arthritis, G. C.	6
No report	32
Total	158

Consider first the group with acute gonococcal urethritis. They were about equally divided between white and colored, and the age varied from 15 to 72 years. Of the 65 cases in this group, 49 were having their first infection and 16 were either reinfections or recurrences. We were interested to ascertain whether or not the duration of the urethral discharge before treatment began affected the result. As shown in *Chart 4,* 78 per cent of the 9 patients treated within two days after the onset were cured; 95 per cent of the 12 who began treatment within two to seven days after the onset were cured. There were 44 who had had their discharge over a week, and of this group 87 per cent were cured. We should conclude from this that the patient who starts treatment a week after the onset of his discharge has an equal chance of being cured with one who begins treatment earlier. This observation, which is contrary to that made in instillation treatments, is the same reported by Cokkinis,[6] of London, in his series of 250 cases. The rapidity with which this drug acts upon the patient is indeed most astonishing. Many patients notice the disappearance of the discharge as early as 12 to 24 hours after beginning treatment. In *Chart 5* we have grouped these cases according to the cessation of the urethral discharge. All of the acute symptoms of urethritis also disappear, usually within

Chart 4

Duration of U. D.	U. D. Present	Relation to Result Per Cent Cured
Two days	9	78
Two to seven days	12	92
Over one week	44	87

Chart 5

CESSATION OF U. D. IN ACUTE URETHRITIS

	Cases
Second day	21
Third to fourth day	25
Fifth to seventh day	4
Eighth to fourteenth day	3
Twenty days	2
Six weeks	1
Total	56

Symptoms cleared with cessation of U. D or earlier, usually in twenty-four hours.

the first 24 hours. Approximately 85 per cent of the cured cases were cleared of their symptoms and urethral discharge within the first four days after beginning treatment and half of these were cleared within the first 24 hours. However, while the vast majority of the patients cleared up very rapidly, there were a few who took several days, one 20 days, and the longest six weeks before a cure was obtained. Because of these findings we are inclined to believe that if the patient does not show marked improvement within the first four days, he is apt to be one who will not respond favorably to the drug. We do not, however, agree with Cokkinis in stopping the drug at this time because there are some who take longer to clear up.

One is naturally most interested in the toxic manifestations which may be expected from the use of this new chemotherapeutic agent. Recent literature is full of these untoward reactions. In this series practically all patients had lassitude, general ill feeling, and slight dizziness. They often stated that they felt just as if they were on a "light drunk," and quite irresponsible and disoriented at times. A few automobile accidents have resulted from taxi drivers under the influence of this drug. Practically all patients also showed a definite cyanosis in the form of light blueness of the lips and nail beds; only 12 in our series had marked cyanosis. The bloods in all these patients were examined for methemoglobin and in only three was it over 5 mg. per cent;* the highest was 20 mg. per cent. In these three cases the drug was stopped, although we do not think now this is an absolute reason for discontinuing it. The average blood sulfanilamide concentration in these three cases was 10 mg. per cent, which is definitely higher than the average in the series.

The presence of sulfhemoglobinemia also has been noted. Discombe has reported 8 cases and suggests the possibility of using a pocket spectroscope for detection, as we do here. There has been one death reported in the *Lancet* which was thought to be due to sulfhemoglobinemia. Marshall recently has doubted the presence of sulfhemoglobinemia in the blood and does not think that it is true sulfhemoglobin. However, it is suggested that sulphates are contraindicated during the administration of this drug. All of the bloods were examined for sulfhemoglobin, but it was found present in small amounts in only four. In these cases the blood sulfanilamide concentration averaged 6 mg. per cent. Many of our patients had slight nausea and 17 of them marked. In none was it severe enough to discontinue the drug. Three cases, however, had vomiting; in these the blood sulfanilamide concentration was markedly elevated, as noted in *Chart 6*. In only one case was the drug stopped because of vomiting. Slight headaches are common and of little significance, but severe

*In practically all of our cases new methemoglobin is reported present.

Chart 6

Reaction	Number of Cases	Blood Sulfanilamide Concentrated	Number of Cases in which Drug was Stopped Because of Symptoms
Lassitude and dizziness	All slight	6.2 average	0
Cyanosis	All slight 12 marked 3 methemoglobin 7 to 22 mg. per cent	All around 10 mg. per cent	3
Sulfhemoglobinemia	4	6 mg. per cent	0
Nausea	Many have slight 17 rather marked	3 to 6 mg. per cent	0
Vomiting	3	11.2 mg. per cent 9.2 mg. per cent 6.5 mg. per cent	1
Headache	Many have slight 15 severe	6.2 average	0
Skin rash	4 on sixth to fifth day	7.5 1 case	3 1 dosage lowered
Edema of face	2		
Fever	2	7.8 mg. per cent	2

Chart 7

OTHER REACTIONS REPORTED IN LITERATURE NOT ENCOUNTERED IN THIS SERIES

Nitritoid crisis—Borst

Acidosis—Southworth, two cases

Hemolytic anemia—Janeway and Kohn, three cases; Colston, three cases; Hb. and W.B.C. every 24-48 hours

Optic neuritis—Bucy, on small dosage for three days cleared up next day

Agranulocytosis—Young, one case; Borst, one case; Long, three cases, one died; Plummer, one case, died; Trumper, two cases, well; and Mitchell, one case, died.

Chart 8

RESULTS

	Per Cent Cases	Cures	Remarks
Dees and Colston	47	78	Acute urethritis
Herrold	14	33	Gave only 1.3 gms. Q.D.
Buchtel and Cook	31	87	Acute urethritis
Orr	134	85	No division into acute and chronic
Authors'*	65	86	Acute urethritis
Reuter	100	90	Acute urethritis

*Since reading this paper our series has increased to 95 cases with 76 per cent cures. We feel that this lowering of the per cent cured is due to the fact that the majority of our cases now coming into the clinic have received sulfanilamide and are in that group which does not respond well to the drug.

headaches, of which there were none in this series, may be an indication for stopping the medication. Skin manifestations are not infrequently encountered in the form of erythematous blotches, urticarial wheals, or maculopapular eruptions. Curiously enough, these reactions have occurred on the parts of the body exposed to the sun. Many of our patients, being farmers, have come in with a rash over the forearms and hands, back of the neck and the face; this localization has also been noted by Newman and others. Newman[20] suggested that sulfanilamide is a photosensitizing agent of the skin. In this series there were four patients who showed this toxic reaction between the fourth and sixth day. Blood sulfanilamide concentration in these patients averaged 7.5 mg. per cent. In three of these cases the drug was stopped because of the severe reaction; and in one the dosage was lowered and the rash disappeared. In two of our cases associated with the rash there was edema of the face, lips, and eyes; and in another there was an asthmatic reaction as well. This has been reported by Salvin,[24] who thinks that it is a hypersensitivity, often associated with itching and sneezing, which can be relieved by the injection of epinephrine. One of our patients was so relieved. It is possible, he says, to do a skin test with sulfanilamide to detect the sensitive patients.

Schonberg[25] reports a most interesting case of a man who had a rash over his whole body with a temperature of 104° on the fourth day of treatment. He received only 3.5 grams one day and 1.5 grams for three days. The drug was then stopped and it took several weeks before the rash faded. This is unusual, for the rash ordinarily will disappear in a few days after the drug is stopped. Later he tested out this patient with one tablet and he immediately developed a scarlatiniform rash with edema of the eyelids and lips. Evidently the patient was highly sensitive to the drug. Newville reports four cases of maculopapular rash in parts exposed to the sun, associated with fever, chills, and leukocytosis. Orr had six cases of urticaria. Skin manifestations, particularly when associated with elevation of temperature, are a definite indication for stopping the drug. In our series two patients had a sharp rise of temperature and in both of these patients the drug was discontinued, although the blood sulfanilamide concentration was only a little higher than the average. One must use utmost care in deciding whether the elevation of temperature is due to the disease for which we are giving the drug or to the drug itself. If it appears on the fifth to the eighth day, when the temperature has previously been normal, it most likely is a reaction to the drug. Hageman[11] reports elevation of temperature in 21 cases in 134, the temperature rising as high as 104°. Nine patients had associated skin eruptions appearing on the third to the fifth day. The relative infrequency of this reaction in our series may be explained by the fact that the large majority of our cases were out-patients. The two that did come under our observation were in the hospital. Acidosis has been suggested as a common finding, but in our series this was not evident. We have had many in which we suspected acidosis, but found that the carbondioxide combining power was within normal limits. Southworth[26] reports two cases of acidosis coming on between the second and the sixth day in which the carbondioxide combining power was 36 and 27 per cent. Long thinks that this is due probably to an absolute loss of sodium and potassium in the urine. For that reason he has suggested and we have given 2 grams of sodium bicarbonate three times a day along with the drug. Other reactions noted have been nitritoid crisis reported by Borst,[2] and optic neuritis reported by Bucy.[4]

Perhaps the most serious reactions one is apt to encounter are damage to the blood system in

the form of hemolytic anemia and granulocytopenia. In the Johns Hopkins Hospital, Long has seen 12 cases of hemolytic anemia and six of them had an associated jaundice. They all recovered on the usual treatment of liver extract, and in only a few cases were transfusions necessary. Janeway and Kohn[13] report three more cases without a fatality. In over 400 cases reported by Orr, Reuter, Colston, and ourselves, there was no such complication. The occurrence of agranulocytosis or granulocytopenia is probably of more serious import. Plummer[22] reports one fatal case; Trumper,[27] two cases which were cured; Mitchell,[19] another fatal case; and Long has had three cases, two of which recovered. He feels, however, that the one fatality was probably due to the incorrect usage of the drug. Blood reactions are sufficiently frequent and severe to necessitate repeated checks on the hemoglobin and white blood count. A marked decrease may be noted in either within 48 hours. In summary, then, in our series the drug was discontinued in only five cases because of a toxic reaction. In one instance the dosage was lowered because of a skin rash; it was stopped in one on the fourth day because of nausea; in two, because of cyanosis with methemoglobin of 11 and 14 per cent; in one, because of a mild anemia and in another because of headache and fever. In 20 cases the drug was discontinued before the completion of two weeks of therapy, varying from four to ten days from the beginning, because the patient was entirely well and there was no recurrence. It may be proven that it is not necessary to continue the drug at the dosage that we now recommend in order to attain a cure; it may be better to lower the dosage and continue it for some time after the discharge has disappeared. Additional experimentation will settle these questions.

Dees and Colston, in their report of 47 cases, had 78 per cent cured; Buchtel and Coop reported 31 cases with 87 per cent cured; Orr reported 134 cases, 85 per cent cured; and Reuter 100 cases, with 90 per cent cured. In all these reports there was no division of the cases into acute and chronic. Herrold[12] gives the only discouraging report, 14 cases with only 33 per cent cured. However, in his series he gave the patient only 1.3 grams per day, which we believe to be an inadequate dosage. In our series of 65 cases of acute gonococcal urethritis, 56 or 86 per cent were cured. It is, of course, most important to explain just what is meant by a cure. Our criteria were that the patient have no urethral discharge, no symptoms, clear urine in the three-glass test and no white blood cells or gonococci microscopically in the centrifuged urine specimen. All of our cases were controlled by blood sulfanilamide concentration determinations and the attempt was made to keep the concentration above 6 mg. per cent. Reuter reports 92 per cent cures in patients treated within two weeks of the onset of the disease and 88 per cent cure in cases older than two weeks. His average length of time for cure was 5 days. The discharge in one of his cases cleared up after taking sulfanilamide only 24 hours, at which time the drug was stopped. The discharge reappeared in 12 hours. Following a second administration of sulfanilamide for 24 hours the discharge stopped and there was no recurrence. Many of our cases have cleared up within 24 hours, but with the exception of the 21 cases reported above we have continued the drug over the usual two weeks period. Two patients received the drug for only four days and had no recurrence. Colston has suggested that we must expect recurrence of the disease in from 5 to 10 per cent of cases. In our 56 cures there were only three recurrences and they cleared up completely on the second course of sulfanilamide. It has been suggested that sulfanilamide might destroy the natural immunity which the body builds up against this disease, but this has not proven so. We have had a case that was entirely cured in three days and had no signs of infection for a period of three months. Five days after another definite exposure he developed acute urethritis, which we feel was a reinfection and not a recurrence. This second infection cleared up promptly and there has been no recurrence to date. There have been some communications in the British journals, particularly by Whitby[29] and Anwyl-Davies,[1] which were disappointing; but Erskine, Johnson and Lloyd[9] reported 73 per cent of cures. They have suggested that we supplement sulfanilamide with local urethral instillations. Summarizing the results from five different clinics, covering several hundred cases, the percentage cures range from 78 to 90.

The results have been so uniformly good that at present we are more interested in the failures, of which there were 9 in this series. As stated above, the drug is broken up in the blood into two forms, the free or the active sulfanilamide and the conjugated or acetylated, which is supposed to be the inactive form. The drug is excreted in the same two forms in the urine.

It occurred to us that perhaps the reason for the failures was too low a blood sulfanilamide concentration. It was this idea which stimulated us to determine the blood concentration routinely in all our patients. Several hundred determinations have been made. In *Chart 9* we have recorded the nine unimproved cases with their blood free-sulfanilamide determinations. The average was 4.8 mg. per cent in this group as compared with the cured group of 6.2 per cent. The difference is so slight that we are inclined to believe that this is not the solution of the problem; particularly since many of our patients cleared with a concentration as low as 2.5 or 3 mg. per cent. However, some patients did not react favorably on the usual dosage, but did respond on increased dosage which raised their blood concentration level. Evidently some individuals need a higher concentration of the drug in the blood in order to obtain a cure. Others in whom we have raised the blood level to as high as 10 to 13 mg. per cent have not been cured. It occurred to one of us (W. D.) that perhaps some individuals inactivate a higher percentage of the sulfanilamide. As stated above, the usual relative proportion of the free and the acetylated forms is as 4 to 1. In this group of cases the relative proportion has remained the same, so that we feel that the failures cannot be explained on this basis. Experimentally it has been shown that the acetylated form is the inactive one and not potent in curing the infection. It has been recently reported that urine obtained from dogs who have been treated with sulfanilamide has more potent bacteriocidal properties than untreated dogs' urine to which sulfanilamide has been added to the same concentration. Therefore, perhaps there is an unknown substance with bacteriocidal properties which is formed in the body by the administration of sulfanilamide. On the other hand, it is possible that the high per cent of free sulfanilamide in the dog's urine may be responsible for the increased bacteriocidal power.

Chart 9

UNIMPROVED CASES

No. Cases	Average Blood Sulfanilamide Mg. Per Cent		Treatment Followed for
	Free	Conj.	
1	4.7	1.5	21 days, reaction
1	3.0	1.5	14 days, no return
1	6.3		14 days, no return
1	4.5		40 days, no return
1	4.2		60 days
1	7.5		30 days, no return
1	4.0	1.	Three months later reinfection Treated for three weeks, unimproved
1	6.0		16 days, no return
1	3.0		8 days, no return

Average blood sulfanilamide (free) of this group, 4.8 mg. per cent

Three of our cases which we intend to report later are particularly interesting in that they failed to respond to sulfanilamide therapy although the dosage was practically doubled and the blood concentration rose as high as 14 mg. per cent. Two of them cleared upon the administration of disulfanilamide.

UNIMPROVED CASES

Case 49142.—A patient with acute urethritis of two days' duration was put on a dosage of 6 grams the first day and 2.7 grams for fourteen days. Blood sulfanilamide concentration on the second day was 6 mg. per cent. He was followed two weeks and there was no change in the urethral discharge and the stained smear was still positive. This patient was simultaneously taking neoarsphenamine in the Syphilis Clinic.

Case 90792.—A patient with acute urethritis of one day's duration was given 6 grams of sulfanilamide the first day and 3 grams every day after that for two weeks. Blood level on the seventh day was 6.5 mg. per cent, and on the fourteenth day 6.2 mg. per cent, certainly a sufficiently high concentration. In spite of this there was no change in his infection. He did not return.

Case 81745.—A patient with acute urethritis of one day's duration had had three months previously a similar infection treated with sulfanilamide and cured immediately. From his history and examination of the patient we were convinced that this was an entirely new infection and not a recurrence. He was put on 3.6 grams the first day and 1.8 grams for the following eleven days. The blood level was 3.2 mg. per cent on the second day. The sulfanilamide was raised after eleven days to 6 grams for one day and then 3 grams each day for two weeks. The free sulfanilamide in the blood was 4.2 mg. per cent, which was 59 per cent of the combined. Medication was stopped for a week and then he was put back on the same dosage of 6 grams the first day and 3 grams each day thereafter for a two weeks' period. In spite of this dosage the blood concentration did not rise above 4.2 mg. per cent. The sulfanilamide was administered for a total of six weeks. The urethral discharge was definitely less, but was still positive for gonococci. This is a most interesting case in that the first infection cleared up very rapidly and then three months later he developed a new infection which did not respond to the drug.

Case 19530.—A patient with acute urethritis and prostatitis, recurrent over a period of 15 years, came in complaining of pain in the right scrotum. Urethral smear was positive for gonococci and he was put on the usual 6 and 3 grams. The acute epididymitis did not respond as usual, but the swelling continued with abscess formation. After a period of three weeks of the drug, the patient developed a rather marked cyanosis and pallor. Hemoglobin was 65 per cent, white blood cells 12,250.

The drug was stopped. Blood levels during this time were 6.2 mg. and 4.7 mg. per cent, representing 76 per cent of the free form. The urethral discharge entirely cleared up, but the pus aspirated from the abscess in the epididymis showed gonococci.

Case 91387.—Acute urethritis of three weeks' duration was complicated by trigonitis. The usual dosage was given for one week, at which time the blood level was 4.4 mg. per cent. The urethral discharge continued and gonococci were present. The trigonitis improved markedly. This patient took the drug for only one week. A week later he reported to another clinic in the hospital and a note was made there that the urethral discharge was still present.

Case 88190.—A patient with acute gonorrheal urethritis of two weeks' duration had taken sulfanilamide, two tablets, three times a day before admission. He began with 6 grams the first day, 4.5 grams the second, and 3 grams a day after that. Blood levels were 13.5 mg. per cent on the ninth day, 2.5 mg. per cent on the thirteenth day, and 7.4 mg. per cent on the twenty-first day.

Case 90727.—A patient with acute gonorrheal urethritis received 4.8 grams of sulfanilamide the first day and 2.7 grams the second day for 34 days. Blood levels were 3.1 mg. per cent on the third day and 4.5 mg. per cent on the tenth day. The urethral discharge decreased, but there were still gonococci present. He was followed for 40 days and a urethral discharge containing gonococci persisted.

Case 89521.—A patient with acute urethritis of one month's duration was given sulfanilamide in the usual dosage for five weeks, in spite of which the blood sulfanilamide level ranged around 2.5 mg. per cent. After discontinuing the drug for a week it was started again on a larger dosage (6, 4.5 and 3 grams) and continued for another five weeks, during which time the blood sulfanilamide level could not be raised above 6.1 mg. per cent. As the urethral discharge persisted and intracellular diplococci were still present, the patient was admitted to the hospital and given sulfanilamide 6 grams the first day, 4.5 grams the next day, and 3 grams daily thereafter. On this dosage the total blood sulfanilamide level was raised to 12 mg. per cent, 80 per cent of which was in the free form. The total urine sulfanilamide level was raised to 230 mg. per cent, 65 per cent of which represented the free form. These levels are certainly sufficiently high, but, nevertheless, the infection was unchanged. Sulfanilamide was discontinued and after three days' intermission disulfanilamide was administered, giving 6 grams the first day and 3 grams daily thereafter for six days. His discharge immediately stopped and the urine was cleared of white blood cells and bacteria. The patient was discharged as cured nine days after beginning disulfanilamide therapy. He returned to the out-patient department twelve days later and examination showed there had been no recurrence.

Chart 10

RESULTANT COMPLICATIONS

Goldstein reported 1000 cases treated locally with 42 per cent complications

Colston	150 cases treated with sulfanilamide
Reuter	100 cases treated with sulfanilamide
Orr	134 cases treated with sulfanilamide
Buchtel and Cook	31 cases treated with sulfanilamide
Cokkinis	250 cases treated with sulfanilamide
Crean	100 cases treated with sulfanilamide
Authors	65 cases treated with sulfanilamide
	830 cases with NO complications

The question naturally rises, in these unimproved cases, whether some individuals conjugate a higher percentage of the sulfanilamide. Perhaps the failures may be explained on this basis. In our failure group the average level of free sulfanilamide in the blood was slightly lower than in the cures. This was not always true, however for one case had a concentration of 10 mg. per cent, only 20 per cent of which was conjugated sulfanilamide. Furthermore, we have had several patients who have taken small amounts of sulfanilamide before admission; these individuals did not seem to respond so well to the larger doses. Is it possible that they have accustomed themselves to conjugating sulfanil-

Chart 11

Cases	No. Cases	Well	Improved Cases	Unimproved
Acute urethritis	65	56, or 86 per cent		9, or 14 per cent
Chronic prostatitis and urethritis*	30	15, or 50 per cent	12, or 40 per cent	3, or 10 per cent
Acute prostatitis	4	3, or 75 per cent	1	0
Acute trigonitis	10	8, or 80 per cent	2	0
Acute epididymitis	6	5, or 83 per cent	1	0
Paraurethral gland	5	5, or 100 per cent	0	0
Arthritis	6	Focus, 2 Joints, 1	Focus, 2 Joints, 4	Not recorded, 2 No change, 1

Since reading paper this group has increased to 45 with the same relative percentages.

amide into the inactive form, and hence can take larger doses without obtaining a high blood level of the free form? These patients do not seem to have severe toxic reactions. It is the general concensus that a high blood level should be obtained on the first and second day of treatment. It is possible that the organism can build up an immunity to the drug when given in small doses and later be able to withstand larger doses. All of these questions and others are most interesting and open up a vast field for chemotherapeutic research.

We began the study of sulfanilamide treatment of the complications of gonorrhea several months ago. To our surprise we found that we were not receiving as many of these cases in the clinic as formerly. The census of the last six months as compared with the previous six months showed a 50 per cent decrease. Since then it has shown a 75 per cent decrease. This is easily explained when we consider that physicians throughout the country have recently been using sulfanilamide for the treatment of gonococcal infections. Practically all of the complications we now see are in patients who have not been treated with sulfanilamide. Many years ago Goldstein reported a thousand cases of acute urethritis of which group 42 per cent developed complications before they were cured. In contrast to this report is the present series of over 800 cases reported by five men in which no complications have been observed. This is indeed a most striking difference. However, it is only reasonable to suppose that some of these patients who do not respond favorably to this therapy will develop complications.

A study of a group of the complications of acute gonococcal urethritis is presented. There are 30 cases of chronic prostatitis and chronic urethritis, 4 of acute prostatitis, 10 of acute trigonitis and posterior urethritis, 5 of acute epididymitis, 5 of para-urethral gland infection, and 6 cases of acute gonococcal arthritis. Conjunctivitis and vaginitis are also included. In the first group consisting of 30 cases of chronic prostatitis and urethritis, our criterion for a cure was that there must be no urethral discharge, no more than 10 white blood cells per high power field in the prostatic fluid, and the urine must be clear in all three glasses. These patients were treated with the same dosage administered to the cases of acute urethritis. In this group there were 15 or 50 per cent well; 12 or 40 per cent showed marked improvement in that the gonococcus had entirely disappeared, but the pus cells remained in a greater number than 10 per high power field in the prostatic secretion; 3 or 10 per cent were unimproved inasmuch as they had gonococci in the stained smear from either the urethra, the prostate or the centrifuged urine.

In this series we had four cases of acute prostatitis. All of these patients came in with enlarged, tense, and tender prostates. One of them was in acute retention and they all had elevation of temperature as high as 102°. They were treated with our usual dosage over a period of two weeks. In all four cases the symptoms of burning, urgency, pain in the prostatic region, and elevation of temperature began to subside within 24 to 48 hours. Within two to three days their temperatures were all normal; and the swelling in the prostates had markedly diminished. One of these cases was entirely normal by the end of two weeks. His prostatic secretion had less than 10 cells per high power field; his urine was clear in three glasses; and there were no gonococci in the stained smear from his prostate or centrifuged urine. Two cases still had pus in the prostatic secretion, but the stained smear was negative for gonococci and the urine had only a very few cells in the first glass. One case showed marked symptomatic improvement and his temperature promptly returned to normal. After a period of two weeks, however, he still had gonococci in the prostatic secretion. In this group 75 per cent of the cases were cleared within two weeks.

There were ten cases of acute trigonitis and posterior urethritis. Our criterion of a cure in these patients was that the symptoms were relieved, and no pus or bacteria was found in the centrifuged urine. Accordingly, eight were considered well and in two cases pus and bacteria continued to be present in the urine. In almost all cases the burning, frequency, and urgency cleared up rapidly, usually within 24 to 48 hours after the treatment was begun.

There were six cases of acute epididymitis. In this group 5 or 83 per cent were considered well and one improved. In all the cases the fever disappeared within 24 to 48 hours and most of the pain was relieved in the epididymis in 48 hours. The acute swelling was markedly diminished at the end of 24 hours and the epididymal mass gradually subsided over a period of two or three days. By the end of a week the swelling in all of them was almost entirely gone and there remained very little scarring, enlargement or induration. Probably the most

striking feature of this group was the rapid disappearance of the pain and fever. There was a patient who came in with an early epididymitis; although he was put on sulfanilamide, a small localized abscess formed. This was aspirated and injected with 2 per cent mercurochrome. The abscess promptly healed, but the gonococci continued to be present in the urethral discharge. Four cases of epididymitis are reported by Herrold and two by Buchtel in which there was rapid improvement and little residual scarring.

There were five cases of para-urethral gland and duct infection. These infections had been present from three months to four years. In all these cases the infection entirely cleared up, the swelling disappeared, and there was no discharge from the duct or urethra. There has been no return of these signs although some of these patients have been followed as long as three months. In two of them the discharge stopped on the second day; in three, on the third or fourth days. The urethral smears were correspondingly negative in two cases in two days, two in three days, and one in eight days. In all the patients the first glass urine specimen was clear and the smear negative for gonococcus.

The six cases of acute gonorrheal arthritis were not on the urologic service. These patients were not followed with blood concentration levels as carefully as the others so that no definite conclusions may be drawn. We have divided the results into two groups: first, the result obtained in the focus of infection; and second, the result obtained in the involved joint. In two cases the focus entirely cleared up with negative smears, no discharge, and clear urine. In one of these cases the joints were well; in the other, it was slightly improved. Four other cases showed marked improvement. In two cases in which the focus improved there was practically no discharge, but the gonococcus was still present in the centrifuged urine. This series must be better controlled with blood concentration levels, temperature reactions, and joint cultures before a definite opinion can be given on the results in gonococcal arthritis.

The Pediatric Department has treated several cases of gonorrheal conjunctivitis which have cleared up promptly and completely on sulfanilamide therapy. Dosage was controlled by blood concentration determinations. In the treatment of vaginitis in infants there was one permanent cure in five cases. In some of the other four, the discharge cleared up, but two weeks later the gonococcus could still be found in the vaginal smear. This is also often the case in vaginitis in adults. Why the drug should not clear up the infection in the vagina as effectively as it does in the urethra is still an open question. These conditions need further and more intensive study.

SUMMARY

(1) A brief review of the introduction of sulfanilamide and its experimental and clinical application are given.

(2) The physiology and pharmacology of the drug are described.

(3) The mode of action of the drug is discussed.

(4) The importance of the blood concentration level is emphasized.

(5) Methods for determination of the blood concentration of the free sulfanilamide, methemoglobin and sulfhemoglobin are given.

(6) Factors determining the blood sulfanilamide concentration level are discussed.

(7) The clinical toxic manifestations of the drug are described.

(8) Presentation of the results in 158 cases of gonococcal urethritis and its complications are reported.

(9) Our results corroborate the few previous reports; 86 per cent cures are obtained in acute urethritis according to very definite and strict criteria.

(10) Significance of the blood concentration level in the cures and the unimproved cases is discussed.

(11) Does the inability to conjugate the drug determine its effectiveness?

(12) Summary of the unimproved cases is given.

(13) Two of the unimproved cases were cured by disulfanilamide.

(14) Results in the complications of gonococcal urethritis are presented.

CONCLUSIONS

(1) Sulfanilamide is the most potent drug for the cure of gonorrhea and its complications at our disposal.

(2) It should not be dispensed over the counter by the druggist, but should be given only by a physician who will watch his patient most carefully for toxic manifestations.

(3) A definite blood concentration is desired and must be obtained before one can claim a failure of the drug.

(4) The exact or best dosage is still an open question.

(5) A combination of sulfanilamide plus anterior urethral instillations of an antiseptic, or hyperpyrexia, may possibly be superior to the drug alone, and may be indicated in certain cases.

(6) The explanation of some of the failures may be low blood concentration levels or the ability of the individual to conjugate a higher percentage of the drug. Many of the failures remain unexplained.

(7) Sulfanilamide and its allied chemical compounds open up a vast fertile field for chemotherapeutic research.

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DISCUSSION (*Abstract*)

Symposium on Sulfanilamide—Papers of Drs. Clark and Branham, Dr. Ainsworth and Drs. Alyea, Daniel and Harris.

Dr. Henry S. Browne, Tulsa, Okla.—Whenever a new drug proves to be of great therapeutic value it is apt to be exploited. Such is the case with sulfanilamide, which is insoluble in water and alcohol, but was dissolved in diethylene glycol by a drug house and detailed to the profession as the first preparation of it that could be taken in liquid form. Following its use deaths began to occur in various parts of the country, and it was later shown that these deaths were due not to the dissolved sulfanilamide, but to the solvent, diethylene glycol. We were unfortunate enough to have in Tulsa nine children and three adults who died. I was called in consultation in all of the adult cases, and shall give a brief review of my observations.

All patients became ill after taking from sixty to one hundred c. c. of the so-called elixir. The first symptoms were nausea and vomiting, followed by severe pain in the region of the kidneys and complete anuria. The temperature did not go above 100.6° or the pulse above 110. The respiration was normal until a few hours before death, when it became labored with great air hunger, not relieved by oxygen. Leukocytosis varied from 15,000 to 23,000 and hemoglobin was 85 per cent in all three cases. Nausea and vomiting persisted throughout; one patient had diarrhea and the two others were constipated. Treatment, in brief, consisted of forcing fluids and then eliminating them by sweating and purgation. One patient died twenty-four hours after admission, four days after anuria developed. One had anuria for seven days, then voided 3,500 c. c. in three days before dying. The last patient had anuria for seven days, then voided 700 c. c. in the twenty-four hours before death. The urine in both cases, except for a moderate amount of albumin, a few red cells and pus cells, was negative. There were no casts. The non-protein nitrogen and creatinin in all cases was high and continued to increase even after the urinary function was reestablished.

The pathological findings in brief by Dr. I. A. Nelson, of St. John's Hospital, were as follows:

All organs except the kidneys and liver were essentially

negative. The gross appearance of the kidneys was not uniform in the different cases. They were about twice the normal size. There were usually areas of purplish mottling and in some cases more extreme changes with cortical necrosis. The cut surface showed the purplish mottling to be due to areas of hemorrhagic infarction reaching the cortical surface from the mid-cortical zone, where they first occurred. One kidney showed no gross vascular changes at all, thus proving that they were secondary. Microscopic examination showed the characteristic change to be a swelling or ballooning of the cells of the proximal portion of the convoluted tubules with a reduction in the size of the nuclei. The glomeruli were normal. There was no leukocytic or round cell infiltration and no hyaline degeneration. The livers were pale, yellowish, and not greatly enlarged. Their edges were sharp and the lobules distinctly visible. Microscopically the cells around the central vein showed the same characteristic ballooning with the nuclei greatly reduced in size. The inner foamy structure was very distinct. Chemical tests showed no increase in visible fat or glycogen in the liver or kidney cells, which we know will cause ballooning of the cells.

From the fact that in two of these cases the urinary function was reestablished, yet the blood nitrogen continued high and even became higher, the evidence points to the liver dysfunction as the primary cause of death. The function of the kidneys was reestablished, but the livers were too badly damaged to maintain life.

To Dr. I. A. Nelson is due the credit for the early recognition of this condition, which galvanized the American Medical Association and the United States Government into action, so that every bottle of this "elixir" was traced to its ultimate destination and confiscated.

Dr. John M. Pace, Dallas, Tex.—Drs. Clark and Branham, Ainsworth and Alyea are to be congratulated for their most interesting and instructive papers on sulfanilamide. This drug is probably the forerunner of many advances in the field of chemotherapy, and it is not at all unlikely that the advent of sulfanilamide will ultimately be considered as important as Ehrlich's discovery of arsphenamine.

Sulfanilamide is our most valuable single drug in treating urinary tract infections. It exerts a remarkable bacteriostatic and in some instances a bacteriocidal action against all of the organisms commonly encountered in the urinary tract with the exception of the *Streptococcus fecalis*. This single and peculiar exception was recently called to our attention by Helmholz. In contrast to mandelic acid this drug has a greater bacteriocidal action in an alkaline urine, a fact of considerable clinical importance as smaller doses of the drug may be employed provided the hydrogen-ion concentration in the urine is maintained well above pH 7. As would be suspected, sulfanilamide has proven to be indispensable in combating the urea splitting organisms which have been little affected by the other drugs at our disposal.

The series of cases reported and the results obtained by Dr. Ainsworth are most impressive. The value of sulfanilamide in treating gonorrhea in the male is well recognized and it should be regularly employed in controlled patients. It is hoped that the profession will in some manner be able to prevent its indiscriminate use by the laity.

Dr. Alyea has presented extremely valuable data and we trust that he will be able to continue his investigations. Additional knowledge of the action of sulfanilamide, other than in the urinary tract, is highly desirable.

Dr. D. W. Branham, Oklahoma City, Okla.—In order to interpret statistical data compiled for the purpose of determining the curative effect of any particular drug in the treatment of gonorrhea, it is necessary, first, to have a clear conception of what constitutes a cure. From our experience it is evident that sulfanilamide is a drug that markedly changes the clinical picture of gonorrheal infection to the point that signs and symptoms are decreased or even eliminated entirely and unfortunately, in too many instances, without completely eradicating virulent organisms. Such a "masking" effect is not only important from a public health standpoint, but makes it extremely difficult to appraise its clinical effectiveness from the standpoint of producing a complete cure. Time alone is the dictator that determines whether a cure has been accomplished, and even then our conclusion is often presumptive. In the light of this knowledge it is obviously a most difficult problem to say that the drug is efficacious to a curative degree, particularly in the earlier weeks of infection.

Certainly this medication will be found a valuable adjunct in reducing not only the clinical intensity of gonococcal infection, but also the number of complications that often result. Aside from its use in gonorrhea we have found it not a panacea so far as other nonspecific tract infections are concerned, although often effective when failure is encountered with other methods of treatment. Properly used it has proven a valuable addition to our list of drugs useful in urinary antisepsis.

A COMPARATIVE REVIEW OF THE USE OF ANTILUETIC DRUGS IN THE TREATMENT OF CONGENITAL SYPHILIS IN CHILDREN*

By JOSEPH YAMPOLSKY, M.D.
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At present prenatal treatment of syphilitic mothers has greatly changed the therapeutic problem involved in the treatment of congenital syphilitics. Today numerous patients are seen in hospitals and clinics with only a positive serological reaction and no other signs or symptoms of congenital lues. The risk of death in these patients is not so great as in those whose mothers were not given antiluetic medications and they may not need such a severe course of treatment as those who are born with definite evidence of congenital infection.

In the latter the constitutional disturbances are severe and there is a resulting toxemia from the involvement of practically all the organs of the body. These patients require much more

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*From the Department of Pediatrics, Emory University School of Medicine.

severe treatment than the ones who show no definite signs of this infection.

There still remains a group of what may be termed as late congenital syphilitics. Our primary interest in those cases should be to heal the late lesions as well as possible in order to try to prevent later stigmata of syphilis.

Frank R. Smith[1] has shown definitely through a study of cases of latent congenital syphilis that late symptoms can be prevented from developing if treated intensively by methods which will be described later.

My purpose in this paper is primarily to attempt to evaluate the different drugs used in the treatment of congenital syphilis and, if possible, to suggest a definite course which will tend definitely to heal the lesions present and to a possible reversal of the serological reaction from a positive to a constantly remaining negative.

The standard medications that have been used in this country are primarily those containing arsenic or the heavy metals, bismuth and mercury.

Let us first take up the different arsenical preparations. They are arsphenamine, neoarsphenamine, sulpharsphenamine, silverarsphenamine, bismarsen, "mapharsen" (meta-amino-para-hydroxy phenylarsine oxide), acetarsone and acetyl-gluco-arsphenamine.

Chart 1

Drug	Dosage
Arsphenamine and silverarsphenamine (intravenously)	0.05 gm. per 15 lbs. body wt.
Neoarsphenamine (intravenously, intramuscularly)	0.02 gm. per 3 lbs. body wt.
Sulpharsphenamine (intramuscularly)	0.02 gm. per 3 lbs. body wt.
Bismarsen (intramuscularly)	0.02 gm. per 10 lbs. body wt.
Mapharsen (intravenously)	0.06 mg. per kilogram body wt.
Acetyl-gluco-arsphenamine (intramuscularly)	0.05 gm. per dose

(A) *Arsphenamine* (606).—This drug is not applicable in the treatment of infants and children for the following reasons: (1) it can be given only intravenously; (2) must never be given intramuscularly, and this makes it most difficult to use in young infants due to the difficulty of injecting medications in young infants by the intravenous route; (3) it cannot be given at room temperature; (4) it must be neutralized before injecting; (5) and it cannot be concentrated sufficiently to allow small dosages to be given.

(B) *Neoarsphenamine* may be given both intramuscularly and intravenously. (1) When given intramuscularly half of the dose is given into each buttock. There seems to be little pain and the medication is absorbed very promptly. (2) It may be given at room temperature. (3) It does not have to be neutralized. (4) It is diluted in the dosage of 0.1 gram in 1 c. c. of distilled water and 0.02 gram is given for every three pounds of body weight.

(C) *Sulpharsphenamine* has been used extensively in clinics where congenital lues is treated. It has the advantage of the ease with which it may be given intramuscularly and even subcutaneously. Some clinicians prefer this drug to other arsenicals, but one must always be on guard against abscess formation; and the ease with which neoarsphenamine can be employed, at the same clinic hour, in intravenous and intramuscular injections has led me to believe after twenty years of its use that it is preferable to sulpharsphenamine.

(D) *Silverarsphenamine* may be given only intravenously, and for that reason is of no value in the routine use of arsenical preparations in infants.

(E) *Bismarsen* has been used both in children and in adults, and according to Schamberg and Wright,[2]

> "Bismarsen may be used with safety in latent syphilis and used with the knowledge that its therapeutic value is unquestionable; weekly injections may suffice, although bi-weekly injections are preferable."

This drug has also been used extensively in children. It is given only intramuscularly in cases of intolerance to the arsphenamines. Bismarsen may be a drug that will be tolerated. In my experience I have found this medication to be painful and for that reason I have not regularly used it. It is dispensed in 0.1 and 0.2 gram ampules and is dissolved in 1.5 c. c. of distilled water. A suggested dose would be 0.02 gram for every 10 pounds of body weight.

(F) *"Mapharsen"* has been developed in this country through the laboratories of Parke, Davis & Company. They recommend the dose of 0.05 mg. per kilogram of body weight and the total weekly dosage not to exceed 1 mg. per kilogram of body weight. This medication should be given intravenously. Morgan[3] has recently reported a statistical study of forty cases in which treatment was by means of "mapharsen." His conclusions are as follows:

> "Mapharsen is a safe form of arsenic; it is easily administered; the reaction is mild and can be eliminated by careful attention to the dosage, and the effect on the Wassermann reaction is probably slightly greater than is observed with other arsenical compounds previously

used. The proper standard for treatment of children was established at 0.6 mg. per kilogram of body weight."

He also states that he has not compared this treatment with cases in which acetarsone was used. He believes that this drug is the ideal one to be given intravenously and is opposed to the use of drugs intramuscularly in young children. Sufficient data have not been gathered on the use of this drug in infants and children.

(G) *Acetyl-gluco-arsphenamine* (*"neoiacol"*) used intramuscularly has been highly recommended by Kiss.[4] He states that the drug causes no inconvenience nor any damaging influence on the weight of the child treated, and brings about improvement in pathological symptoms and other signs after two or three courses of treatment. This drug has been used very little in America and should not at present be recommended as a routine method of treatment in congenital syphilis. The average number of injections is from 8 to 12 per treatment, using 5 to 6 grams in the energetic treatments, 3 to 4 grams in the medium and 1.5 to 2 grams in the weak.

Chart 2

DRUG: ACETARSONE (ORALLY)

DOSAGE

First period (7 days)—0.005 gm. (1/13 gr.) per kilogram daily
Second period (7 days)—0.010 gm. (1/7 gr.) per kilogram daily
Third period (7 days)—0.015 gm. (1/4 gr.) per kilogram daily
Fourth period (7 days)—0.02 gm. (1/3 gr.) per kilogram daily
Fifth period (5th, 6th, 7th, 8th, 9th weeks)—0.02 gm. (1/3 gr.) per kilogram daily

Give six weekly injections of bismuth followed by acetarsone or weekly injections of bismuth during the course of acetarsone.

(H) *Acetarsone*, or as it has sometimes been called, stovarsol or "spirocid," has been used extensively both in this country and abroad. The drug employed mostly is a preparation used by Levaditi and Ehrlich.[5] While there have been some reports on its intravenous use in the literature, it has been administered primarily by the oral method in young infants. The drug usually is dispensed in tablet form which, if necessary, can be crushed into a powder. As I have stated in a previous report,

"There are many discomforts attending the use of hypodermic injections and there is no reason why an attempt should not be made to return to oral administration if it produces results similar to those received from intramuscular or intravenous injections."

In my observation acetarsone has proven one of the most valuable additions in the treatment of congenital lues. That has been true not only in young infants, but in cases where patients remained Wassermann-fast following the use of neoarsphenamine and mercury, or neoarsphenamine and bismuth. This medication may be given either once daily or divided into three powders, each powder to be given fifteen minutes before meals in a little water. The dosage is as follows: first period (7 days), 0.005 gram (1/13 grain) per kilogram daily; second period (7 days), 0.010 gram (1/7 grain) per kilogram daily; third period (7 days), 0.015 gram (1/4 grain) per kilogram daily; fourth period (7 days), 0.02 gram (1/3 grain) per kilogram daily; fifth period (fifth, sixth, seventh, eighth and ninth weeks), 0.02 gram (1/3 grain) per kilogram daily. Duration of one active course is 9 weeks. There are occasionally untoward reactions resulting from the use of acetarsone. They chiefly consist of rashes, fever, diarrhea, pyelitis and nephritis. Occasionally there have been reported Herxheimer's reaction, flaccid paralysis and even death as in Abt's[6] case. When the simple reactions appear, a mere discontinuance of the drug for a few days until the symptoms have cleared up is sufficient to permit its further usage.

SUMMARY OF THE USE OF ARSENICAL PREPARATIONS IN THE TREATMENT OF CONGENITAL SYPHILIS

Apparently there are three drugs of value as far as the arsenical group is concerned. They are sulpharsphenamine, neoarsphenamine and acetarsone. Intramuscularly sulpharsphenamine and neoarsphenamine should be the drugs of choice. Intravenously neoarsphenamine should be used exclusively. Some years ago I reported in association with Dr. Klugh[7] the use of neoarsphenamine and mercury intraperitoneally. Neoarsphenamine can be given in the dosage of 0.1 gram to every 15 pounds of body weight in 1 c. c. of distilled water with a dull beveled needle into the peritoneal cavity. This is especially applicable in cases where the intravenous method is not applicable. Our results, so far as healing and failure of causing peritonitis and adhesions, have been fully discussed in that report and the reader may refer to it.

The use of acetarsone, I believe, will become more extensive due to the ease of administration and the excellent results obtained, especially when it is given in combination with bismuth or mercury. I would recommend the use of this drug especially in very young infants and in patients whose serological reactions have remained positive after treatment with other arsenical preparations.

MERCURY AND BISMUTH

(A) Mercury has been used since time immemorial and almost up to this century was ad-

Chart 3

Drug	Dosage
Mercury	
Gray powder, orally	12 to 32 mg. three times daily
50 per cent mercury ointment, inunction	1 grain daily
Mercury salicylate (intramuscularly)	1/2 grain per every 30 lbs. body wt.
Bichloride of mercury or red iodide of mercury (intravenously)	1/2 minim per kilogram body wt.
Bismuth (bismuth sodium tartrate intramuscularly)	3/8 gr. (metallic bismuth) per 30 lbs. body wt.
Bismuth salicylate (intramuscularly)	25 to 100 mg. daily according to age

ministered by mouth only. The preparation employed is gray powder (hydrargyrum cum creta), the dosage being 12 to 32 mg. three times per day. Its inefficiency has been fully proven and due to the many gastric disturbances which this medication may cause in young nurslings it should be discarded. Mercury may also be given by inunction. The drug of choice is the U.S.P. 50 per cent mercury ointment. The amount used daily is about 1 gram and a small portion may be rubbed into different parts of the body. While this drug is efficacious in young infants, it may prove useless unless the treatment is fully carried out according to the physician's directions. Mercury has also been given by rectum in the form of suppositories (mercurettes) and by vapor in the form of a mercury powder. Neither one of these methods is of therapeutic value. When given intramuscularly it is usually given in the form of mercury salicylate in an oil or creamy emulsion. The dose is 0.5 gram for every 30 pounds of body weight. In our clinic this has been a very successful way of using mercury and I have had very few toxic reactions to its use. Intravenously the most common salts employed are 1 per cent solution of bichloride of mercury and the red iodide of mercury in a dosage of 0.5 minim for each kilogram of body weight.

(B) Bismuth as well as mercury can be given both in the soluble and insoluble preparations. However, the former drug can be used only intramuscularly and should never be given intravenously. Even in young infants we find great tolerance for this drug. Aqueous solutions are very applicable when used in combination with acetarsone, and in this way I have used bismuth sodium tartrate (Searle), the dosage being about 3/8 grain of metallic bismuth for every 30 pounds of body weight. When quick absorption and elimination are not desired it is preferable to use the insoluble preparation. These can be given in the form of bismuth salicylate and other emulsions. The dosage is usually from 25 to 50 mg. of metallic bismuth in infants under 1 year of age and 50 to 100 mg. in older children.

IODIDES

Coppolino[8] suggests the use of iodides in late clinical manifestations. He believes that 3 to 7 grains three times daily, depending on the size of the child, will relieve the pains in gummatous lesions and syphilitic periostitis. Certainly these drugs should not be used in early congenital syphilis, as they are of little value.

NEUROSYPHILIS

While some of the drugs described here are useful in the treatment of this stage of syphilis, I believe, with other clinicians, that with the advent of the use of malaria and fever therapy, it is possible that we shall see some improvement in congenital neurosyphilitics. The *Treponema pallidum* is destroyed at 41.5 to 42° C. in one hour *in vitro*, in six hours *in vivo*, and in two hours if the lesion itself is raised to 40° C.

Spekter and McBryde[9] give a summary of patients treated by the high fever therapy method. Others have used malaria, diathermy, tryparsamide and malaria. All these cases were juvenile paretics. The authors were especially impressed with the change of the spinal fluid from abnormal to normal. Of the five cases that the authors reported, in *Case 2* the Wassermann became negative after one and one-half years of fever therapy. Interstitial keratitis seemed to improve with treatment. This method has not been used sufficiently to be of definite value in the treatment of congenital syphilis.

The outlook in general is much worse in congenital than in acquired neurosyphilis. One thing, however, must be emphasized, and in this matter I am in agreement with practically everyone who has treated congenital neurosyphilis, and that is, tryparsamide should never be employed in cases of congenital origin. We are already dealing with a constant possibility of the development of interstitial keratitis, and we certainly should bear in mind that the risk of blindness is too great in patients when this drug is used.

Chart 4

ALTERNATE WEEKLY USE OF ARSENICAL AND METALLIC PREPARATIONS

Drug	Dosage
(1) Neoarsphenamine (intravenously, intramuscularly)	0.02 gm. per 3 lbs. body wt.
(2) Sulpharsphenamine (intramuscularly)	0.02 gm. per 3 lbs. body wt.
(3) "Mapharsen" (intravenously)	0.06 mg. per kilogram body wt.
(4) Mercury (intramuscularly)	
A. Mercury salicylate (intramuscularly),	1/2 gr. per 30 lbs. body wt.
Or red iodide of mercury (intravenously)	1/2 minim per kilogram body wt.
(5) Bismuth (soluble or insoluble	
A. Bismuth sodium tartrate intramuscularly)	3/8 gr. per 30 lbs. body wt.
B. Bismuth salicylate (intramuscularly)	25 to 100 mg. per day according to age

Alternate these drugs weekly for 80 to 90 weeks. Wassermann taken every 3 months. Spinal fluid examination made at end of treatment.

SUGGESTED OUTLINE OF TREATMENT FOR EARLY CONGENITAL SYPHILIS

(A) Alternating treatment[10] by the use of some arsenical preparations such as neoarsphenamine, sulpharsphenamine, or "mapharsen" with mercury or bismuth intramuscularly.

These are alternated weekly for approximately eighty to ninety weeks. The Wassermann is taken about every three months and a spinal fluid examination is made at the end of treatment.

(Chart 5)

LATE CONGENITAL SYPHILIS

(B) The arsenicals as above are not alternated with the metals weekly, but instead the following routine may be carried out:

6 weeks.....Arsenical preparations
6 weeks.....Bismuth or mercury
6 weeks.....Arsenical preparations
8 weeks.....Bismuth or mercury
6 weeks.....Arsenical preparations
10 weeks.....Bismuth or mercury
6 weeks.....Arsenical preparations
12 weeks.....Bismuth or mercury
5 weeks.....Arsenical preparations
15 weeks.....Bismuth or mercury

EARLY CONGENITAL SYPHILIS

(A) Acetarsone may be used in the following manner. The course consists of seventy-five weeks of treatment, alternating nine-week courses of acetarsone and six weeks course weekly of bismuth injections for five consecutive periods of fifteen weeks each. That means, nine weeks of acetarsone followed by six weeks of bismuth.

LATE CONGENITAL SYPHILIS

(B) Seventy-two weeks of acetarsone, using acetarsone daily and dividing it into eight periods. This is done in order that the acetarsone may be used gradually up to the highest number of grams and then resumed again at the end of nine weeks with beginning of small doses. Once a week these patients are given an injection of bismuth. That means, each patient receives seventy-five injections of bismuth and seventy-

Chart 5

Duration	Drug	Dosage	Remarks
1 to 6 weeks	Neoarsphenamine	0.1 gm. per 15 lbs. body wt.	
	Sulpharsphenamine	0.1 gm. per 15 lbs. body wt.	
	Mapharsen	0.06 mg. per kilogram body wt.	
6 to 12 weeks	Bismuth or Mercury	3/8 to 3/4 gr. 1/2 to 1 gr.	Wassermann taken
12 to 18 weeks	Arsenical preparations	Same	
18 to 26 weeks	Bismuth or mercury	Same	Wassermann taken
26 to 32 weeks	Arsenical preparations	Same	
32 to 42 weeks	Bismuth or mercury	Same	
42 to 48 weeks	Arsenical preparations	Same	Wassermann taken
48 to 60 weeks	Bismuth or mercury	Same	
60 to 65 weeks	Arsenical preparations	Same	
65 to 80 weeks	Bismuth or mercury	Same	Wassermann and spinal fluid examination taken

After 80 weeks of treatment discontinue treatment, see patient from time to time for 6 months, and then follow up patient up to puberty.

five full weeks of the use of acetarsone. The serological examinations are done in the same fashion as reported in A.

It would be advisable in cases of late congenital syphilis or in cases where the serological reaction remains positive to use method B, that is, first, alternate arsenicals with bismuth or seventy-two weeks of acetarsone in which are included weekly injections of bismuth for the same period of time.

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EXPERIENCES WITH METAPHYSEAL GROWTH ARRESTS*

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Popular interest in the leg length problem was initiated by Abbott's making leg lengthening a practical procedure. A dozen years ago, even before his[1] article appeared, we became dissatisfied with our results in the rather formidable technic required in this hazardous procedure and gradually developed a femoral shortening operation which, after several years of trial, one[2] of us published in 1935. This technic has not been materially changed for the last five years and, although it is far simpler than the leg lengthening operation, we readily added to our armamentarium in attacking the leg length discrepancy problem, Phemister's[3] idea of bringing about a premature union of the epiphysis to the diaphysis. As stated in the femoral shortening paper, it is felt that, except in extremely few instances, the leg lengthening principle is fundamentally unsound, and we are only too glad to find some other method, less radical even than the shortening operation, that could be of use in this problem.

While the conception of bone lengthening was not new with Abbott, or shortening with the authors, Phemister can be credited with originating the metaphyseal growth arresting procedure. We are indebted to them for calling our attention to the practicability and usefulness of these ideas. For a good many years prior to our doing these arrests, we had been particularly interested in progressive bone growth deformities from metaphyseal disturbances and gradually collected a group of cases that constituted an exhibit at last winter's Academy of Orthopedic Surgeons meeting in Cleveland. This work is so closely related to intentional metaphyseal arrests that it fits in very well with this subject, and several cases showing some of our earlier patients were included in this group.

The usefulness of the growth arresting technic is necessarily limited to children in whom there may be expected a growth period of several years' duration. However, if considerable inequality in length is to be compensated for in a few years before full growth is anticipated, two or even three of the growth regions of the lower leg may be operated upon, to double or even treble the effectiveness of the single metaphyseal arrest at the distal end of the femur. Thirty-two of the fifty-seven cases in our series were between the ages of 9 and 12, inclusive.

With the premise presumably adequately proven that all longitudinal growth in the femoral, tibial, and fibular diaphyses is the result of metaphyseal activity, the certainty of the elimination of this growth function by the premature fusion of the epiphysis with the diaphysis will not be further emphasized, and we shall proceed with a brief description of the simple technic of this operation.

By using what is known in the wood worker's trade as a square mortising chisel, the procedure is considerably shortened and made more accurate. This tool is made to function as an apple corer, and the only change that needs to be made

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in it to make it suitable for this operation is to file the inside of it square so that the plug of bone that is removed will be injured as little as possible. An obturator of a length of rod large enough to fit loosely the opening through the chisel must also be provided. The purpose of the latter is to drive out the plug of bone, including a section of the epiphyseal line, with a minimum of injury to it. The half-inch square chisel is the ideal size for this work. It may appear to be a little small, but most of these operations are done on children, as stated above, 8 to 12 years of age, and a larger instrument could not conveniently be employed.

The distal epiphyseal line of the femur is approached through two adequate longitudinal incisions, one medial and one lateral, centered over the transversely running line. This is usually located about on a level with the middle of the patella. The fascia on the lateral side is very tight unless the knee is flexed a little, and the periosteum will be found to be firmly adherent to the bone on both sides. It will be well to do the operation under a tourniquet in order to increase the visibility of the parts as the small articular vessels are numerous and bleed freely. If a tourniquet is used, these arteries are too small to be tied.

In order to make it possible to retract the periosteum and place the chisel satisfactorily, about an inch or so of the epiphyseal line should be exposed, as the periosteum should not be cut transversely. We feel this to be quite important, as the lateral ligaments attach just about where the plug is most conveniently removed. After an adequate exposure of the surface of the bone is made, where the white epiphyseal line can be seen transecting it, the square mortising chisel is made to straddle diagonally that structure, so that two of the diagonal points are forced into the line and two into bone on either side. The younger the patient, the wider is this line, but also the smaller is the individual, so we have never seen a case where there was a question as to whether enough bone had been included in the plug.

The chisel placed as described above is then driven into the femoral condyle to a depth of three-quarters of an inch or so, depending, of course, on the size of the child. As the chisel is driven in, it should be directed distally very slightly so as to follow closely the more superficial portion of the metaphysis as it curves downward, paralleling the articular surface of the epiphysis. The somewhat downward direction of the metaphyseal plate can be more accurately ascertained by probing it with an ordinary straight skin needle. After it is loosened, as one would loosen a post that is to be pulled out of the ground, it can easily be extracted, bringing with it the included bone plug in the same manner as an apple is cored. The square plug is allowed to remain in the instrument until it is time to reinsert it, so as to avoid drying. With a fine curette the metaphysis is then erased as thoroughly as possible, particularly the proximal portion. Usually the two plugs on either side come close to meeting and the short space between is broken down with the curette. This latter is not necessary, however.

When sufficient damage has been done to the metaphysis by the curette, the plug is removed from the instrument and replaced in the square hole, rotating it through an angle of ninety degrees, so that the contained portion of the epiphyseal line will be directed in the long axis of the leg and solid bone will bridge across the metaphysis. It is tapped gently into place and the wound closed. A light plaster is employed to immobilize the leg for a fortnight, after which physiotherapy is started and weight bearing allowed in four weeks. The convalescence lasts, at the most, only six to ten weeks and we consider it as a relatively minor procedure.

In all our series of cases, we feel that we have always been successful in producing an osseous bridge across the metaphysis on both sides of the bone, and therefore arresting growth. We have been on the lookout for a case where the operation has been a success on one side of the leg and a failure on the other. No deforming growth has been noted to persuade us to think that this has occurred, and we have therefore been led to believe that the technic described above has been adequate. We have felt that the technic originally described by Phemister was not always adequate and so have modified it as per the above.

In all, fifty-seven cases have been plugged and of these, one-half of them have been done so recently as to warrant no conclusions as to their success. The first patient was done approximately three and one-half years ago and observation on a sufficient number of these older cases allows us to feel justified in making this favorable report on the procedure as a whole. In about one-half (twenty-eight) of the total number of cases, the discrepancy in length was due to anterior poliomyelitis. The next commonest cause was congenital deformities (eleven), and a poor third, namely, six cases, was due

to either malunion of the femur or osteomyelitis involving the metaphysis. One-half of all of the earlier group of cases were associated with femoral shortening procedures. Triple plugging operations, that is, arrests upon the three metaphyseal plates about the knee, were done on four; the upper metaphyseal plates of the lower leg were done in only two cases, for the sake of maintaining symmetry of the level of the knees. In one case each, the metaphyseal plate of the fibula or the tibia was done separately, because of bone growth disturbances, and of course were associated with an osteotomy of the other bone, the tibia in the case where the fibula was arrested, and the fibula where the tibia was arrested.

A majority (twenty-nine) of these operations were done on patients with a residual anterior poliomyelitis paralysis, where disturbance of the trophic centers varied tremendously. For instance, we have had patients where there was complete recovery from the paralysis, but serious retardation in growth, as well as others with little retardation in growth, and serious permanent paralysis. The patients for whom it is easiest to plan are those where, because of some pathological process, a single metaphysis has been destroyed and the corresponding growth center on the opposite extremity must be eliminated, instituting leg shortening or leg lengthening procedures in addition, if this is necessary.

It is quite difficult to calculate the amount of correction that may be expected, particularly in the polio cases, from metaphyseal arrests, but I feel that it is quite safe to figure on between one-quarter and three-eighths of an inch a year during the growth period, except in those cases where all three metaphyseal plates have been operated upon, in which instance twice the corrective action can be expected.

The periods of relatively accelerated growth vary so with the different cases that we have found it impractical to give much consideration to it. It is well, however, to pay some attention to the height of the parents and at what age they had ceased growing. Harris has some interesting data on growth spurts, but we have found that one's experience is the best guide.

In conclusion, therefore, from our acquaintance with this procedure, we have found it to be a valuable principle which we have added with great satisfaction to our armamentarium available for the treatment of the short leg.

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DISCUSSION (*Abstract*)

Dr. Joe H. Boland, Atlanta, Ga.—Inequality in leg length is a crippling deformity and may result from a variety of causes. So far most procedures have been of a corrective or compensatory nature.

The best treatment of any medical or surgical condition is prophylaxis. The prophylactic measure must be without risk of life and without risk of causing a more serious condition than that which would have resulted if the measure had not been undertaken.

The production of metaphyseal arrests does answer the qualifications of a prophylactic for inequality in leg length. The technic is simple and Dr. White has added to the simplicity. The convalescence is short and free of pain. With reasonable accuracy we do know what to expect as a result of the procedure.

My experiences have naturally been fewer than those of Dr. White. The two problems which have given me most concern when the question of metaphyseal arrests arose were, first, the time to operate. My experiences have been entirely with polio cases and there is no way of foreseeing the amount of shortening which will result. Second, is the obtaining of permission for operation. Parents are hesitant about having a good leg operated upon when one leg is already affected. This may have been due to the fact that I did not explain the procedure clearly or that the parents lacked confidence in me.

Dr. Alfred R. Shands, Jr., Durham, N. C.—The equalization of leg length is always a fascinating subject. Dr. White has been a close student of the various procedures now for ten years or more. The shortening of the long leg has been his primary interest. He undoubtedly was the first to demonstrate the practicability of shortening the femur. It had been done sporadically over a great many years before his time, but now it is considered always when an operation is contemplated to equalize leg length.

The technic of his femoral shortening is simple. The technic demonstrated today of arresting epiphyseal growth is simple. The results of both procedures are certainly worth while.

A word of caution must be sounded. In spite of the simplicity of the operation, it is not one for every surgeon to undertake. A careful study of the cases beforehand and an accurate and careful follow-up until the growth periods have ended are absolute necessities for the success of the procedure. The operation is distinctly still in the experimental stage. The end result studies of the cases do not extend over a sufficient period of years to warrant an absolute opinion on the value of the operation.

Dr. White has been a pioneer in this field of orthopedic surgery. I hope that eventually this procedure may become standard.

Dr. Earl D. McBride, Oklahoma City, Okla.—Dr. White has certainly given us valuable information on the subject of epiphyseal arrests. It is an advantage to all of us that one man will continue to gather statistics and publish his observations on a subject which is of technical uncertainty to those of us who have not done a great many cases.

It is my observation that in closing the epiphysis and attempting to equalize the length of legs there is an effect on the pelvis, spine and general posture as a whole. The x-ray records that Dr. White has shown of his cases indicate that the postural relationship of the remainder of the body has not been so accurately recorded as the local parts affected by the epiphyseal arrests.

I wish to suggest that the use of ruled screens and 36 x 14 inch x-ray plates, such as I devised for registering the progress and measurement of scoliosis cases, would apply also to the progress of epiphyseal arrests in the lower extremities. With these plates the patient's standing posture may be obtained and will register on the plate the head, entire trunk, and most of the lower extremities. Of course, this requires a special casette which is somewhat expensive, but it seems to me in orthopedic surgery we should advance to use such plates in cases where the entire posture is affected. We should cease relying upon inaccuracies of photographs and shadowgraphs when it is necessary to register the entire postural development of the body.

Dr. J. Albert Key, St. Louis, Mo.—One of the principal reasons why more arrests of the epiphyses are not done is that we still have no standardized method of determining how much an individual is going to grow. I wish that Dr. White and others who are doing much of the work on equalization of the length of legs would attempt to formulate some definite rules in regard to expectancy of growth which the rest of us can follow.

I should also like to know how frequently Dr. White can depend upon acceleration of growth in an extremity which has been shortened by an osteotomy. We know that in treating fractures of long bones in children there is a tendency for a small amount of shortening to be corrected by an acceleration of growth, but sometimes this does not occur, and in an individual in whom we expect the short leg to catch up with its fellow it remains short. I should like to know how frequently this occurs and how much gain in length may be expected in the average case.

Dr. White (closing).—We have never had any real difficulty in obtaining permission from the parents to operate upon these cases. Most of the patients upon whom this operation had been performed had been under observation for a number of years and the children were admitted as a matter of course to the hospital with rarely any discussion with the parents about what was to be done. From the start we have been in the habit of taking the parents into our confidence, which fact possibly prevents serious objections on their part.

Dr. Shands mentioned the importance of accurately recording leg length. We, ourselves, feel that although the graphic method which we have described is not entirely accurate, it is a real necessity in a study of this nature.

We do not feel that the more elaborate tele-roentgenographs suggested by Dr. McBride are necessary and, after making hundreds of leg length x-rays, are perfectly satisfied with the simple technic described in this paper. While this report must still be considered as a preliminary one, we are of the opinion that any orthopedic surgeon can go ahead with assurance, using the data obtained in this study.

As time goes on, we find that we are doing fewer leg shortening or leg lengthening procedures, as we more and more appreciate the value of metaphyseal arrests.

In answer to Dr. Key's inquiry about what may be expected in the way of spontaneous correction of leg length discrepancies following fractures, our experience has been that no more than half an inch compensatory overgrowth of the short injured leg can be expected. If a chronic osteomyelitis persists, however, following a compound fracture, this serves as a continued stimulus and as long as any inflammation exists, growth will be faster than on the other side. Adequate spontaneous correction, in other words, of a serious amount of discrepancy following fractures, such as two inches, cannot be counted on. We are of the opinion that in various studies of this matter, erroneous measurements were taken which led to unjustifiable conclusions. We are referring particularly to David's article which appeared in the *Archives of Surgery* in 1924.

As to the use of the pavex machine to stimulate growth in the short leg, we feel that the idea is well conceived and that stimulation will result from its use over a period of several years. Unfortunately, this is ordinarily impracticable, but along that line we are glad to report that we have a series of six cases in which it is hoped that growth will be stimulated by deep x-ray therapy. We have often thought where growth stimulation of one leg was indicated, that the wearing of an electric heating pad every night about the knee would produce a stimulative hyperemia.

Once more, may we thank these gentlemen for their generous discussions and assure you all that the cases included in this paper will be kept under continual observation and will be reported upon again in a few years. We have found the problem a most fascinating one and hope that many others will be encouraged to work up a similar group of cases.

CHRONIC ULCERATIVE COLITIS*

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Chronic ulcerative colitis may be defined as an inflammatory disease of the colon accompanied by diarrhea with blood, mucus and pus in the stools, abdominal pain and a variety of symptoms referable to other organs. Although it is not a common disease, it is certainly not infrequently encountered. It seems unusual that relatively little has been written about this disorder, the etiology being unknown, the course usually debilitating and prolonged and the outcome fatal to many.

Sydenham[1] was probably the first observer to describe accurately certain symptoms of the disease, for, in 1669, in writing of a sporadic case, he says:

"These slimy motions appear with streaks of blood,

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*From the Roosevelt Hospital, West Fifty-Ninth Street and Ninth Avenue, New York, New York.

though not always; sometimes indeed, there is no passage of blood whatever from first to last. Notwithstanding, provided that the motions are frequent, slimy, and attended with griping, the disease is a true bloody flux or dysentery."

Jean Cruveilhier,[2] in his "Anatomie Pathologique" of 1835 to 1842, vividly portrays cicatrization of intestinal ulcerations, and particularly ulcerations which are the result of acute or chronic follicular enteritis. Allchin,[3] before the Pathological Society of London in 1885, presented a specimen of classical and extensive ulceration of the colon, the process being limited to the large intestine; there were numerous large ulcers which presented a clean base, and in places consisted of scarcely more than peritoneum; they

"vary in size from one and a quarter inches to scarcely more than a mile. The mucous membrane over large areas was denuded, showing the subjacent muscle tissue. The bowel contained dark, blood-stained, grumous, feculent material and masses of mucus. As he relates, this case both in its clinical history and in the pathological specimen presented, corresponded in all of its details with what was at that time called 'follicle ulceration of the colon.'"

The above description is one of the earliest accurately recorded in the literature.

This disease is characterized pathologically by inflammation and ulceration of the colon, by infiltration and marked scar tissue production in the deeper layers of the colonic wall, and at times by secondary anatomic changes in other tissues. It is characterized physiologically by profound disturbances of function of the stomach, the small intestine, and the colon, which contribute importantly to many of the symptoms and which condition the appearance of certain important complications. The disease tends to run a long-continued chronic course with periods of exacerbation and spontaneous remission.

It has been considered to be a local infection of the colon. A variety of different organisms have been advanced as etiologic agents. In recent years the statement has been made that chronic ulcerative colitis results from infection by a specific organism.[4] This contention has not been fully accepted. Certain studies are rather convincing that present evidence does not support the thesis for a single infectious agent.[5] Cultures from rectal mucosa frequently repeated over prolonged periods of observation have demonstrated a varied bacterial flora. Among the potentially important organisms are: unidentified strains of Salmonella; Shigella dysenteriae; *beta* hemolytic streptococci; paratyphosus A; paratyphosus B; and the Morgan bacillus No. 1.

MECHANISM

Continuous clinical observations of these same patients point to a mechanism which involves factors in addition to simple infection of the colonic wall.[6] Both primary and secondary infection are admittedly important, although in many instances no recognized pathogenic organisms can be recovered on culture.

Many of the severe cases are complicated by mixed deficiency states which develop under hospital conditions and despite what should be a normally protective diet.[7] They are accompanied by characteristic changes in the small intestine demonstrable by x-ray, which are identical with those observed in sprue.[8 9] These changes have both diagnostic and prognostic significance. The importance of early recognition and appropriate treatment of the deficiency states cannot be over-emphasized.

Dietary studies, the effects of autogenous vaccine overdosage, and analysis of the apparent causes of exacerbation or recurrence indicate an important factor of intestinal allergy in many instances. Repeated use of the test diet method of investigation has given definite clinical evidence of active food allergy in 51 per cent of the cases studied. Frequently, however, evidence of sensitivity to a specific food is obtainable only intermittently in a given patient. This necessitates repeated diet studies before the potential role of this factor can be evaluated.

The frequent association of upper respiratory infection with exacerbation or recurrence of the colitis, and the focal reactions produced by overdosage of autogenous vaccine, point to sensitization of the colon to bacterial protein.

PHYSIOLOGY

These varied factors of primary and secondary infection; bacterial and food allergy; and secondary or conditioned deficiency disease, are accompanied by physiologic disturbance of the gastro-intestinal tract which tend to create a vicious circle. Gastric anacidity is common. Hypomotility of the intestine is more common than is generally appreciated. Particularly in the severe cases abdominal pain and profuse diarrhea may be associated with stasis in the proximal colon, a point of major importance in the clinical management of the particular case.

DIAGNOSIS

Is it possible that segmental enteritis, regional ileitis, colo-ileitis and chronic ulcerative colitis are various forms or stages of one and the same pathologic entity? Whether this may or may not be true we do know that chronic ulcerative

colitis in the majority of instances (probably 90 per cent) starts in the rectum and extends upward, often involving the entire large bowel. A ten-year experience in the treatment of this disease at the Mayo Clinic revealed that in 1,348 cases the entire colon was involved in 64 per cent, and that in 17.5 per cent of the 866 cases represented by the 64 per cent, the terminal part of the ileum was also involved; anus to hepatic flexure 6 per cent; anus to splenic flexure 11 per cent; in 15 per cent only the rectum and sigmoid; a regional involvement of disseminated patches of the colon, 4 per cent.

Positive diagnosis is made by proctoscopic examination and by the x-ray. It seems hardly necessary to emphasize the importance of immediate rectal examination with the finger and sigmoidoscope and the use of a barium enema in any person discharging blood and mucus from the anal opening.

The x-ray findings in chronic ulcerative colitis show narrowing, shortening, mucosal destruction and absence of haustral markings (it is well to remember that such a picture is seen in any ulceration of the colon), which usually begins in the rectum and progresses proximally. There is a diffuse symmetrical involvement of the circumference of the bowel with thickening of the wall. The contour of the mucosa is usually smooth when the ulceration is granular and superficial, but when the ulcerative process extends deeper the mucosal destruction is more severe, the contours are uneven, fringed and feathery. There is rapid falling of the bowel with the rectal barium enema and hyperirritability of the involved segments. The course of the bowel has a tendency to lose its gently twisting character and normal angulations at the flexures, tending to approximate right angles.

INDICATIONS FOR SURGERY

Except for impending perforation, massive hemorrhage, multiple skin infections, crippling joint symptoms, continued anemia and loss of weight and strength, surgical measures should be delayed until two factors have been definitely evaluated:

(1) The response to conservative management.

(2) The extent of permanent damage to the colon.

It is needless to state that before any of these patients are subjected to the risk of surgical interference, meticulous study over a relatively long time should be insisted upon. Any variance of fundamental physiology should be corrected. The diet must be carefully studied and deficiency states combated. If predominant pathologic bacteria are recovered on cultures, autogenous vaccines should be given a thorough trial.

When other medical measures such as rest in bed, high caloric, high vitamin, low residue diet, irradiation of focal infections; multiple transfusions simple and irradiated, a recent suggestion that aluminum hydroxide in kaolin mixtures be used, when all these things have failed and this patient may be classed as suffering from intractable chronic ulcerative colitis, then and only then is surgery definitely indicated.

SURGERY

Up until the last decade surgery has played a minor role in the treatment of this disease. Ileostomy has been used by many as a curative measure, but it was soon learned that this surgical maneuver was only palliative and certainly not curative. There is no question that it is a life-saving procedure in the acute fulminating phases of the disease. We have all seen patients after ileostomy gain considerable weight; yet experience has proven that they have not been thoroughly and completely cured until the diseased colon was removed. Ileostomy itself is attended with a high mortality due to the rapid loss of fluids and chlorides. In fact, we believe that there is a higher mortality attending this relatively simple surgical operation than is seen following the second stage when practically the entire colon is removed. We strongly advise a transfusion directly following ileostomy and 3,000 or 4,000 c. c. in twenty-four hours of saline intravenously for many days postoperatively.

Ileo-sigmoidostomy in a small percentage of cases is warranted, if it is understood that the diseased bowel at a later time shall be removed. The end-to-side method is the only one that assures a complete diverting of the fecal flow.

Total colectomy has been done by various surgeons throughout this country and abroad only a relatively few times. In 1931, Rankin[11] reported six total colectomies without a fatality for complicated chronic ulcerative colitis and its sequelae, and for polypoidosis; and he later added five cases[12] in which total extirpation of the colon was carried out, three of which for the familial variety of adenomatosis and two for chronic ulcerative colitis.

Cattell,[13] of the Lahey Clinic in Boston, has done sixteen total colectomies with removal of the rectum and six partial colectomies for chronic ul-

cerative colitis. His only fatality was in a patient who died in the hospital five weeks following the second stage from sepsis due to the presence of the diseased lower segment still remaining. His mortality following ileostomy was 22 per cent, which is an excellent example of how cautious one should be in giving a prognosis following this simple maneuver.

At the Mayo Clinic[14] forty colectomies have been done for chronic ulcerative colitis.

Our own interest in the surgical management began in February, 1936, hardly two years ago. Our experience has been sufficiently large to warrant but few conclusions, and sufficient time has not elapsed to report on the late results in these cases. We are, however, convinced of the dangers of ileostomy and we are certain that the removal of the entire colon is less of a formidable procedure than is generally supposed; we are impressed by the smooth convalescence which follows the removal of the large bowel which we feel is due to two factors: (1) a careful preoperative preparation and (2) the fact that sufficient self-immunization has occurred due to the presence of the diseased colon over a long period of time.

Total colectomy is carried out in three stages, sometimes four, as has been done by Cattell: first stage, transverse permanent ileostomy; second stage, removal of the remaining ileum, entire colon down to the juncture of the sigmoid and rectum; third stage, removal of the lower sigmoid segment, rectosigmoid and rectum by combined abdomino-perineal resection.

We believe it essential to transfuse these patients during or immediately after each of these three stages. Up to the present time we have removed the entire colon and rectum in two individuals, two patients have had subtotal colectomies following ileo-sigmoidostomy, one has had the ileostomy done, subtotal colectomy carried out and is waiting for the removal of the lower sigmoid and rectum. One other has been given a transverse colostomy with removal of the entire descending colon and is waiting for the removal of the lower sigmoid and rectum. All of these six patients have been females; all have suffered from the disease for over three years. Medical management has been meticulously carried out and has failed to effect a cure; all have had exceedingly smooth convalescence; there have been no fatalities.

COMPLICATIONS

Some of the more common complications of chronic ulcerative colitis are the development of strictures, hemorrhage perforation with ensuing localized or diffuse peritonitis, perirectal abscess, skin diseases, thrombophlebitis and polypoidosis. Adenocarcinoma has been known to develop on existing polyps which have been the result of chronic ulcerative colitis.

CONCLUSIONS

The contention that chronic ulcerative colitis is due to a specific organism is not accepted. There is apparently a mechanism which involves factors in addition to infection of the colonic wall. Many of the severe cases are complicated by deficiency states. Positive diagnosis can be made by bacteriologic studies, roentgenograms and proctoscopic examinations.

Except for the acute emergencies, surgery should not be instituted until two factors have been evaluated: (1) the response to conservative treatment; (2) the extent of permanent damage to the colon. Ileostomy, though seemingly a simple surgical maneuver, is fraught with grave dangers. The three- (and occasionally four-) stage procedure we believe to be the safest surgical measures of effecting a cure, due to a prolonged self-immunization from the presence of the diseased bowel and to careful preoperative preparation. The risk of colectomy is not tremendous.

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THE ROLE OF SURGERY IN PEPTIC ULCER*

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Less than a quarter of a century has brought about a gradual but radical change in the management of uncomplicated peptic ulcer. Little has been added to the etiology of the disease, but definite progress has been made in the methods of treatment. In the early days of accurate diagnosis by the x-ray, it was generally felt that ulcer once established meant cure by surgery. There followed a widespread use of surgical procedures to bring about what was believed to be a better physiological situation by means of turning back into the stomach the alkaline contents of the duodenum. An anastomosis between the stomach and jejunum became the most popular of these procedures, because it was technically easy and did give, on the whole, encouraging results. The various pyloroplasties ran a close second, and to offset the increase in technical difficulties they had in addition to functional points in their favor the removal of the ulcer in many cases. The most popular of these is that devised by Finney, although similar operations such as gastroduodenostomy as advocated by Wilkie have received considerable support. While the surgeon has been trying to evaluate these procedures, the internist has ended the controversy so far as the simple uncomplicated peptic ulcer is concerned by developing a regime on which the patient may live comfortably without surgery. This is based largely on the common sense management of rest, peace of mind, bland food, and alkalies. To this treatment acute ulcers yield with such gratifying results that surgery has become an unnecessary procedure except in those cases where complications have taken place. It seems reasonable to suppose that better understanding of the pathology of acute ulcer may eventually lead to a complete solution of the problem by protecting all individuals along psychiatric, hygienic and dietary lines, particularly as regards an adequate intake of vitamin C.[1] Therefore, in time we may be able to avoid first the acute ulcer, then its recurrence, and finally its chronic state, which brings about the complications that at present must be handled surgically.

In a study of end results on ulcer patients treated surgically in the Massachusetts General Hospital prior to 1923, Fremont-Smith and McIver[2] found that posterior gastroenterostomy gave approximately 80 per cent of relieved patients over a period of time varying from 2 to 10 years. That some of these individuals later became ill as a result of their original ulcer or the surgery done to relieve it is a known fact. On the other hand, in the past 15 years 80 per cent of those individuals with proven duodenal ulcer who came to this same hospital for relief were made symptom-free and had their ulcers disappear in the x-ray film on a conservative regime. Without doubt, this discrepancy in results by the two methods of treatment is due to a number of factors. The tendency of ulcer to be precipitated by worry and emotional strain, its apparent association with an excess of acid in the stomach, and knowledge of the effect of highly seasoned foods, alcohol, and tobacco on its development and maintenance, give the internist something upon which to carry forward a logical sequence of measures that allows nature to bring about healing of this lesion. One must not overlook the fact that medical men who interest themselves in this problem can with assurance expect results if attention to detail is carried out with the confidence and cooperation of the patient. Thus, in our hospital a special gastro-intestinal clinic headed by Dr. C. M. Jones has worked out a regime that makes it possible to treat many of these individuals in the out-patient department with a surprising degree of success. This is of particular interest when one takes into consideration the social standing and intelligence of the average patient who comes to the charity clinic of a large urban hospital. The more ill and those who fail to respond to ambulatory treatment, will often lose their symptoms and show a healed ulcer by x-ray examination following a few weeks in bed in the hospital. These, together with all surgically treated ulcer cases, are discharged to their homes, but are followed for indefinite periods in the gastro-intestinal clinic. Being human, they rarely follow their diet and prescribed mode of living to the letter and thus many of them return in varying degrees of recurrence, chronicity,

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*From the Surgical Department of the Massachusetts General Hospital, Boston.

or with complications. The percentage of those who could be classified as relieved would certainly equal or exceed the percentage of those so classified after the palliative surgical procedures thought wise twenty-five years ago. Failures may have been due to lack of understanding of diet and care after operation, since many of these individuals were of the opinion that once they had an operation to relieve their ulcer further restrictions were unnecessary. This lack of proper respect for their ulcer tendency was almost entirely due to our own ignorance regarding the whole situation. The various complications that have arisen following a temporarily successful surgical procedure have accumulated with such impressive magnitude that now the internist persuades the surgeon with some difficulty to help him over an *impasse* in an intractable case of peptic ulcer. Both, however, warn the patient that strict attention to detail as regards his mode of life must be promised after operation or a bad situation may well be turned into a worse one. Thus, regardless of the improvement that may be brought about by surgery in such cases, one must not be led astray by the statements appearing in the literature that if the surgery is radical enough the patient will be symptom-free and able to lead a normal life as regards work and diet. That this may occur in certain cases cannot be denied, but a much safer stand to take is that once an ulcer patient always an ulcer patient, and these individuals can never be told with assurance that they can forget their stomachs regardless of the mechanical procedures that have been carried out upon them.

The small group of ulcer patients who now become surgical may be classified as follows: (1) acute perforation, (2) cicatricial obstruction, (3) profuse bleeding, (4) intractability.

(1) *Ulcers with Acute Perforation.*—Here we may find some individuals who have had little or no warning that an ulcer exists, since there appears to be a definitely silent area in the duodenum and even in the stomach in some of these patients. Therefore, with no previous symptoms of sufficient severity to require attention they are suddenly stricken with a knife-like pain in the epigastrium quickly followed by collapse of such appalling quality that the diagnosis can often be made at first glance. The majority of these patients, however, have had indigestion, have been constant users of sodium bicarbonate, and many have had an accurate diagnosis made by x-ray examination at some previous time. It is generally agreed that such a patient should be operated upon at the earliest possible moment under the best conditions available, as the mortality in these cases is in a direct ratio to the number of hours elapsed between perforation and closure. A few cases with small perforations and those that may be walled off early by nature's method of sealing the opening with some near-by structure may survive if operation is refused or not feasible for obvious reasons. To attempt to select these infrequent cases who may get well without operation is too hazardous at present and one should give them the better chance for recovery by an early intervention. If the diagnosis is in doubt one is justified in operating on strong suspicion, since a diagnostic exploration is far less dangerous than the development of unmistakable signs of full blown peritonitis.

Surgery should be restricted in most instances to a simple closure of the perforation. This is best done by the fixation of a tab of omentum over the opening by means of sutures passed through the ulcer and tied loosely as advocated by Roscoe Graham.[3] Rarely can this be improved upon by attempting to close the perforation by placing sutures in the healthy tissue around the ulcer and tying them together. In a few instances, the closure of such a perforation may apparently occlude the outlet of the stomach or first portion of the duodenum so that a superimposed gastroenterostomy may seem indicated. One must take into account, however, the edematous state of the tissues around the ulcer and realize that as this diminishes sufficient room for the passage of secretion and food will be present. It is generally agreed that to combine gastroenterostomy or pyloroplasty for the sake of curing the ulcer or preventing a recurrence is unjustifiable. In the first place, these maneuvers are apt to be disappointing in attaining the desired end, and in the second place, this added procedure is often enough to tip the scales against recovery in this very ill patient. At present, we feel that the more radical partial or subtotal gastrectomy under these circumstances is unwarranted, since its magnitude will certainly result in a higher mortality in the average case. It must be borne in mind that many patients cure their ulcers by perforation and remain symptom-free after a successful closure for the remainder of their lives.

(2) *Ulcers That Produce Cicatricial Obstruction.*—During the healing of ulcers near the junction of the stomach and the duodenum there

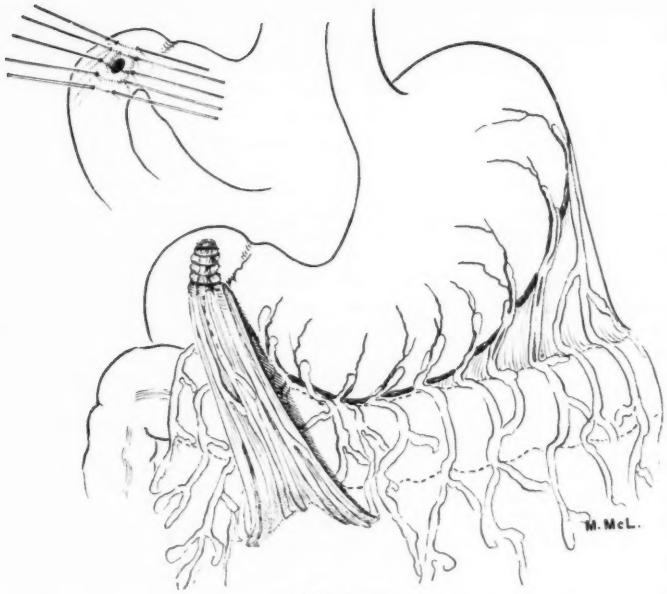

Fig. 1

Diagrammatic sketch of a modification of Roscoe Graham's method of closure of acute perforation in duodenal ulcer. If mesenteric fat tabs of sufficient proximity, size, and freedom with blood supply are not available, a free graft may be used.

comes about the formation of scar tissue. In most instances, this is a small punctate area that causes no narrowing of the viscus and may even be replaced with healthy tissue so normal that it is undetectable on gross examination. With extensive ulceration, however, particularly of the variety that tends to extend in a girdle-like fashion, the scar tissue formation may contract the lumen sufficiently to cause complete stenosis. Multiple ulcers and those of considerable extent may bring about this situation years after the activity of the lesion has ceased. Repeated episodes of activity in an original ulcer or the occurence of new lesions in the same vicinity and increasing scar tissue associated with each flare give a logical background for the development of dense unresilient tissue that finally blocks the passage of secretions and food. This usually takes place after years of ulcer symptoms and may come about following a long period of comfort on the part of the patient. Although this situation can develop in the young and middle-aged, it is far more common in older individuals. Fortunately, in these "burnt out" ulcer patients the acid content of the stomach is apt to be normal or even low. This problem is mainly a mechanical one, so that any form of new communication between the obstructed stomach and high small bowel will be met with success in a very large percentage of cases. Therefore, we feel that in this group radical resection is entirely justifiable.

One must not confuse this chronic cicatricial obstruction with the temporary occlusion often associated with acute or reactivated ulcer. This situation is easily recognized by the symptoms of typical ulcer pain associated with vomiting and will subside as the ulcer heals, provided the stomach is kept decompressed for a few days with the Levine tube. We definitely try to avoid operation under these circumstances, since due to the depleted state of the patient and to the extensive reaction about the ulcer one is limited in the choice of procedures. If operation should be undertaken upon such a patient, it would be wiser to do a conservative one as a preliminary step with the consideration in mind that when the condition of the patient has improved subtotal gastrectomy may be safely accomplished.

(3) *Ulcers Associated with Profuse Bleeding.*—Although it is not generally conceded by the internist that massive hemorrhage from ulcer places the patient in a surgical class, there is considerable evidence to show that on the whole this group is a difficult one to keep symptom-free.[4] This has caused a large number of cases to be looked upon as intractable. This is particularly true, since many patients have recurring bouts of activity, often with hemorrhage of an alarming degree even when they are following to the best of their ability a reasonable regime. Some may get along well if they live the life of an invalid only to find that as soon as they attempt to cope with their regular occupation a return of symptoms appears. Thus, often these patients are considered unresponsive to medical care and so fall into our fourth group, demanding surgical intervention.

From the standpoint of massive hemorrhage alone, we find a logical reason for offering and sometimes urging surgery upon many of these patients. In a careful analysis of 51 deaths

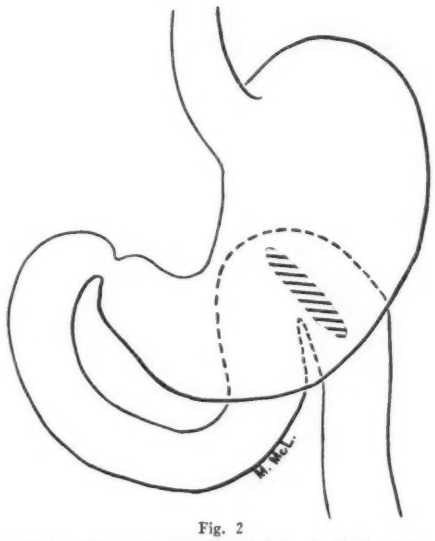

Fig. 2

Posterior gastroenterostomy indicated in cicatricial stenosis. A short loop of jejunum placed with the proximal end of the stoma to the lesser curvature of the stomach is recommended.

from hemorrhage arising in the upper gastro-intestinal tract occurring at the Massachusetts General Hospital in the decade between 1923 and 1932, one of us[5] finds that peptic ulcer was the underlying cause in 21 of these patients. Thirteen of these ulcers were duodenal, 6 gastric, and 2 gastrojejunal. Previously, we[6] have called attention to the fact that in duodenal ulcer fatal bleeding rarely takes place in patients under 50 years of age, while individuals beyond this period of life have a marked tendency to succumb to massive hemorrhage. This holds true in bleeding gastric ulcer as well, although we found that the average age of the fatal cases in duodenal ulcer was 57 as against 52 for gastric ulcer. We believe this age distinction is due to the fact that spontaneous thrombosis is less successfully accomplished in vessels affected by arteriosclerosis than in those of younger individuals. We were not able to show that the duration of the disease, chronicity of the ulcer, or repeated episodes of bleeding, played any definite role in fatal hemorrhage.

Thus, we feel that massive hemorrhage associated with peptic ulcer should always be treated conservatively in any patient under 50 years of age until the victim has entirely recovered from blood loss. Then he should be given a careful regime and should understand that recurrence may take place in spite of anything he can do, but that he may be able to adjust his life in such a fashion that his ulcer will stay healed and so avoid alarming episodes of profuse bleeding with reactivations of the ulcer. If he has made a serious effort to avoid these recurrences and failed, or cannot lose his ulcer symptoms, or finds that he cannot carry on his work, or if he is approaching the age group of fatal bleeding, then he should at a time of optimum election submit to radical surgery.

In rare instances, the surgeon must face radical treatment in the presence of acute massive bleeding from peptic ulceration. In those patients beyond the fifth decade we must consider the fact that death will occur in one-third of them if they are treated by conservative measures. If we wait until death is imminent, usually after a week or more of repeated bursts of considerable blood loss, and then attempt surgery we shall fail in the majority of cases. This is due to the depleted state of the patient. Although we may replace the blood loss by transfusion, we cannot replace the resistance to infection and pneumonia that is present in the individual who has been absorbing nourishment in the normal manner. Thus, in this small group we must make our decision for or against surgery during the first 48 hours of massive hemorrhage. If this is attempted in a logical way, the mortality should be little if at all higher than partial gastrectomy at a time of election. We have previously described[5 6] a method of approach that is useful in dealing with acute massive hemorrhage in duodenal ulcer. One must bear in mind that the vessels leading into the ulcer area must be ligated in normal tissues, and this must be done under vision and in such a manner that

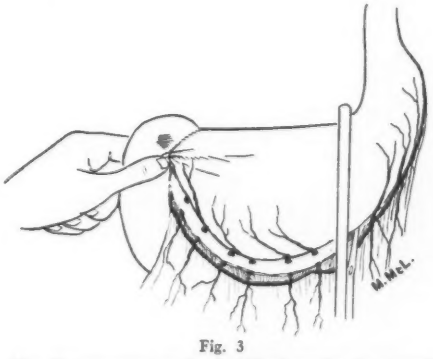

Fig. 3

After the curvatures are freed of blood supply, the stomach is drawn to the right. This makes the stomach more tubular so that all of the cut surface of the proximal segment can be used in the anastomosis, if desired. In ulcer cases the gastroepiploic vessels are spared for better nourishment to the omentum.

blood loss will not take place during the procedure.

(4) *Intractability After Conservative Measures.*—A certain number of individuals with peptic ulcer will for one reason or another fail to respond in the normal manner to so-called medical treatment. A few cannot be made comfortable even on a prolonged hospital regime. Most of them do get better and even lose all symptoms while under careful supervision in bed. A large proportion of this group will do well enough at home afterwards so long as they are removed from psychic disturbances and the strain of business. However, there are some who, regardless of their efforts or the ability of their physician, will continue to be miserable. Some are of a social class that finds it impossible to obtain proper food at home, and even if this can be arranged difficulties arise while they are at work. It has been felt that a few individuals failed due to their own lack of intelligence. Perhaps some should be classified as intractable who, understanding the situation, prefer a gastro-intestinal tract that requires less coddling; they may even refuse to take proper care of themselves on the basis that life is hardly worth while when faced with such rigid rules. A psychiatrist in certain instances is helpful. It is surprising how readily these individuals often accept a hazardous radical operation.

If the surgeon attempts to improve the situation in this group of patients, he is faced with a different problem than we thought existed twenty-five years ago. Then most ulcer patients were considered surgical, and palliative procedures such as gastroenterostomy and pyloroplasty gave a high percentage of satisfactory results. It is possible that the failures then may represent fairly accurately those who fail today to respond to medical measures. Our experience would lead us to believe that palliative surgery will also fail in this group. Since we limit ourselves to a small proportion of all ulcer cases for the reason that only the complicated ones come to surgery, we cannot expect the same degree of success from conservative operations as was obtained when all ulcers were considered surgical. The factors involved in the types that we now believe should be considered in the surgical group must be taken into account. Posterior wall duodenal ulcers associated with bleeding, those with deeply penetrating lesions, multiple ulcers, gastric ulcers that do not decrease in size under treatment, and those who fail to lose their symptoms on conservative management represent a group that need more than a short circuiting operation for relief. Much has been said about the high acidity occurring in the patient with intractable ulcer. So far, little has been said about the lack of this particular individual's natural alkaline resources. We find an increasing interest in associated gastritis, and, with the aid of the gastroscope, Benedict in our hospital is pointing out to us that too little attention has been paid to this factor in the past.

Considering all phases of the subject, we believe now that when operation is undertaken for non-obstructing chronic duodenal ulcer, one should resect a large portion of the stomach. Finsterer,[7] Berg,[8] Lewisohn,[9] Ogilvie,[10] Marshall and Kiefer,[11] Graham,[12] Tomada,[13] and others have advocated subtotal gastrectomy in the past. We feel that the criticisms offered against this procedure are natural, since few of us learn except by our own mistakes and doubtless many of these authors have laid too little stress upon their selection of cases. It is perfectly possible that some of the discrepancies in results from various operations reported in the literature may be due to the varying degrees of gastritis found in different parts of the country.[14] The deductions that we have made have been based on actual experience in a large New England hospital. Many of the patients are of foreign birth and come from the poorer classes. We know that in our clinic any intractable ulcer

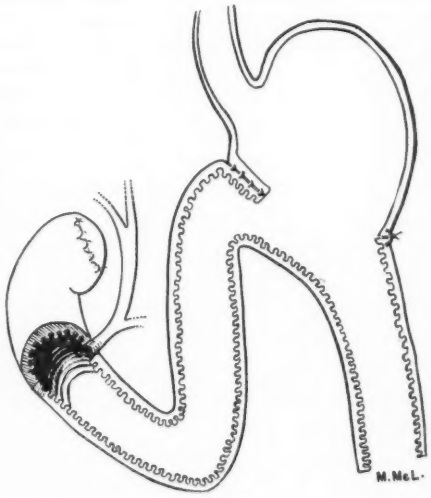

Fig. 4

Traction previously exerted accounts for the remaining segment of stomach assuming its former position. This lends obliquity to the stoma that we believe desirable. The proximal segment of jejunum is carried well up on to the remaining lesser curvature, enhancing the flow of food into the distal limb.

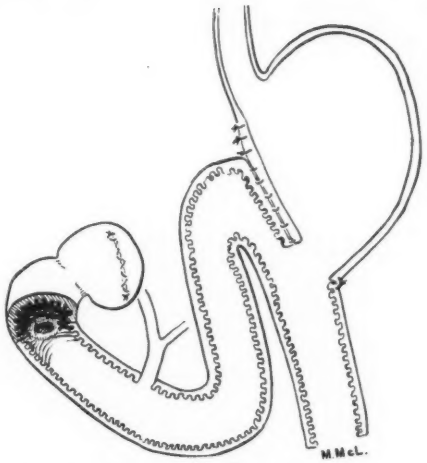

Fig. 5

Finsterer "resection for exclusion." The upper half of the open end of the stomach remnant has been closed; the lower half used in the stoma. The antrum has been transected far enough proximal to the pylorus to allow a comfortable closure.

patient referred to the surgical department by the internist challenges us to radical surgery rather than to a conservative operation. We have tried gastroenterostomy, pyloroplasty, gastroduodenostomy, transsection of the antrum, and pylorectomy, and found too many of these patients returning in a worse state than existed prior to operation.[15] The very fact that one or more operations have already been done makes the more extensive resection harder and consequently more hazardous. If we can bring ourselves to the logical conclusion that this small group of patients is resistant to conservative measures whether these be medical or surgical, we can then proceed with a subtotal gastrectomy with a clear conscience. Gradually, we are accumulating a sizable group of resistant ulcer patients who finally or primarily are symptom-free and working following the removal of two-thirds to three-fourths of their stomach. We have been forced to do this operation as a result of complication or failure following more conservative procedures so often that now we have the courage to carry it out as a primary one in the majority of cases.

We do not think the details of subtotal gastrectomy as varied by different surgeons are particularly important. Whether one closes part of the cut end of the proximal segment of stomach, using the remainder for anastomosis to the jejunum or prefers a long loop anterior rather than a short loop posterior hook-up, probably makes little difference in the final result. We do feel that Finsterer's[16] "resection for exclusion" is a valuable modification in some cases. This is most applicable to the large penetrating duodenal ulcer that is adherent to the pancreas, liver, or biliary passages. It may be well to consider removal of the mucosa of the remaining antrum as advocated by Bancroft.[17] Although the physiology of this procedure may be disputed, it makes the infolding of the stomach remnant easier.

We prefer to carry out subtotal gastrectomy through a left paramedian incision standing on the left of the patient. We begin well proximal to the junction of the right and left gastro-epiploic vessels freeing the greater curvature down to the antrum. This makes it possible to draw the stomach down sufficiently to secure easily the vessels of lesser curvature. Then the stomach is drawn towards the right sufficiently to make it tubular. Strong clamps are placed across it vertically and the organ is divided between them. This gives a narrower proximal segment so that all of it can be used in the anastomosis and the traction previously exerted towards the right allows the remaining stomach to assume a position of obliquity when it is released that we believe favorable to proper function. If the patient is a poor risk or not doing

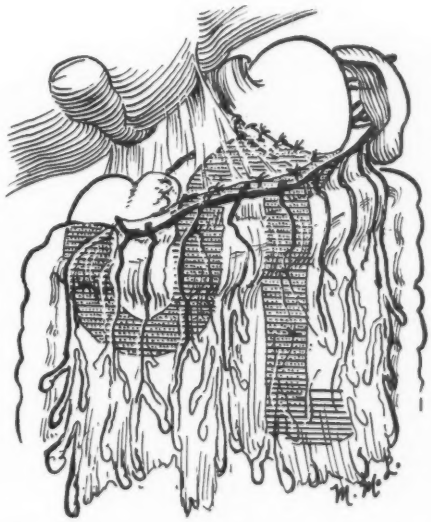

Fig. 6

The rent in the transverse mesocolon has been closed above the stoma to the remaining segment of stomach. The posterior row of sutures is more easily accomplished before the anastomosis is started.

Table 1

DUODENAL ULCER

Massachusetts General Hospital

INCIDENCE

	Treated OPD Alone	Total	Number Surgically Treated	Per Cent Surgically Treated
1922-1926	440	910	211	23.2
1927-1931	322	869	170	19.5
1932-1936	259	947	207	21.7
Total	1021	2726	588	21.5

Table 2

DUODENAL ULCER

Massachusetts General Hospital

INDICATIONS FOR OPERATION

	Acute Perforation	Cicatricial Obstruction	Massive Bleeding	Intractable Pain	Miscellaneous
1922-1926	32	67	6	101	5
1927-1931	55	59	6	45	5
1932-1936	56	67	24	42	18
	143	193	36	188	28
Per cent of total	24.3	32.8	6.1	31.9	4.7

Table 3

DUODENAL ULCER

Massachusetts General Hospital

ULCERS INTRACTABLE BECAUSE OF PAIN OR BLEEDING
TYPE OF OPERATION

	PGE	Resection	Other Operations
1922-1926	87	6	14
1927-1931	37	8	6
1932-1936	20	39	7

Table 4

DUODENAL ULCER

Massachusetts General Hospital

MORTALITY 1931-1936

	Total No. Operations	Died	Per Cent Mortality
Acute perforation	62	17	27.1
PGE	101	8	7.9
Resection	70	11	15.7
Other operations	16	3	18.7

Table 5

GASTRIC RESECTIONS FOR PEPTIC ULCER

Personal Cases 1932-1937

Elective Operations	No.	Died	Per Cent Mortality
Duodenal ulcer	43	2	4.5
Gastric ulcer	7	0	0
Gastro-jejunal ulcer	5	0	0
Total	55	2	3.6

Two duodenal ulcers and 1 gastro-jejunal ulcer operated upon after week or more of massive bleeding, all 3 failing to survive.

well on the table, the anastomosis is done before the distal two-thirds to be sacrificed is removed. The end can be turned in and the removal of this segment accomplished later on at a second stage. We find that dividing the stomach early in the operation is helpful because the posterior surface can then be visualized and the adherent areolar tissue overlying the middle colic vessels behind the antrum can be more safely released. When feasible, the first portion of the duodenum is included in the resection. We have on occasions cut across the duodenum at the junction of an ulcer adherent to the pancreas and depended for closure on suturing the anterior duodenum to the pancreas proximal to the ulcer. Whatever modification one adapts to a particular case depends on the safety and feasibility of carrying out an ideal. We have found the short loop posterior Polya anastomosis satisfactory when the operation is carried out in the above manner. Care is used to start each row of sutures at the upper end of the cut segment of stomach so that the proximal jejunum will be carried well up on the remaining fragment of the lesser curvature. This, we believe, decreases the tendency for food to enter the blind loop of duodenum and does not interfere with the entrance of alkaline secretions at the upper border of the stoma. The rent in the transverse mesocolon is fixed to the remaining segment of stomach above the anastomosis.

The patient is routinely transfused after the operation and he is supported by glucose and salt solution. A Levine tube is left in the stomach until we are sure that liquids are passing freely through the anastomosis, usually a matter of 48 to 72 hours. Water is allowed in sips the day following operation, and this is increased with the addition of milk and lime water the second day. Gradually, feeding is increased and

care is taken to use small quantities at two hourly intervals until a reasonable feeding can be tolerated. The patient is discharged during the third postoperative week on a six-meal bland diet. He is given an appointment to return in one month to the gastro-intestinal clinic. Usually he is able to return to his regular occupation on a liberal diet by the end of the third month. In our opinion, he must always use reasonable care in the use of highly seasoned foods, alcohol, and tobacco.

SUMMARY

(1) Peptic ulcer is primarily a functional disorder responding well to conservative measures.

(2) Complications arise demanding surgical intervention in a definite proportion of cases.

(3) Short circuiting procedures are of value in those with cicatricial obstruction only and should rarely be used for relief of ulcers with other complications.

(4) Subtotal gastrectomy is the logical operation for intractable ulcer and for ulcers that have been associated with massive hemorrhage.

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PHYSIOLOGIC AND PATHOLOGIC REACTIONS OF THE LIVER*

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While very little of the knowledge that has been secured concerning the physiologic and pathologic reactions of the liver can be applied directly to clinical problems, the recognition of the importance of the liver to clinical medicine would appear to justify the presentation of the more pertinent facts regarding such reactions of the organ. In this review, an attempt will be made not only to present some of the more important physiologic and pathologic reactions of the liver, but also to emphasize those hepatic reactions which may be of interest from the clinical point of view.

GENERAL CHARACTERISTICS OF THE LIVER IN RELATION TO PHYSIOLOGIC REACTIONS

The liver occupies a unique position, both anatomically and physiologically, in the body. Anatomically the liver has several characteristics which are of physiologic importance; two of these are outstanding. The liver is the largest organ of the body. This development of a relatively large mass of hepatic tissue is indicative not only of its numerous functions, but also of its capacity for storage. The liver possesses a different type of blood supply than any other tissue of the body. Not only does it have two sources of blood supply, one arterial and one venous, but the venous blood drains from the gastro-intestinal tract and contains most of the beneficial products of digestion as well as numerous other substances which may be of no value to the organism and may even be harmful. Physiologically the liver is characterized not only by its large number of functions and extraordinary functional capacity, but also by the great variability in its functional activity. The liver is truly a dynamic organ. A few of its numerous functions, such as the regulation of the concentration of glucose in the blood, are vital and must be maintained constantly as long as life processes exist. Many of its functions must be coordinated with complex physiologic processes of other tissues of the body. Few of the physiologic processes in which the liver has an integral part

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are completed wholly by, or within, the organ. The physiologic position of the liver demands extremely rapid changes in rate, character and capacity of functional activity. These essential physiologic characteristics of the liver are of importance in the problem of quantitating hepatic function by tests.

HEPATIC ACTIVITY IN RELATION TO METABOLISM

The higher organisms obtain their food at intervals, but their tissues are constantly using food for growth, for repair and for energy to maintain body temperature and mechanical activity. It is obvious that some provision must be made to supply the tissues with food during the interdigestional periods. The most important physiologic mechanisms for furnishing a constant supply of the required amount of usable food reside in the liver.

Storage of Foodstuffs.—While the three major foodstuffs are stored in various tissues throughout the body, the stores in the liver are in general not only relatively larger than in other tissues, but are capable of being more quickly mobilized for utilization.

Carbohydrate is stored in the liver in the form of glycogen which can be quickly transformed into glucose. The latter appears to be the most readily available and most easily utilized of all foods. The amount of glycogen stored in the liver varies within wide limits, but hepatic tissue rarely appears to be glycogen-free. The amount of glycogen which can be stored in the liver is very large and may, under conditions of rapid intake of carbohydrate, reach 20 per cent or more of the total hepatic substance.

It has not been proven that there is a special form of storage protein similar to glycogen as a storage form of carbohydrate, but there is no question that there exists a certain protein content of the liver which is labile and can be used by the other tissues of the body. This labile hepatic protein differs from the protein in the other tissues in the respect that it can be mobilized more quickly and a higher percentage of the total amount available can be utilized. While the body as a whole contains considerable protein which can be used as fuel, the protein in the liver appears to be more readily available. In the fasting state the protein content of all tissues decreases, but the percentage decrease in hepatic protein is not only greater than that in protein of any other tissue, but it occurs more rapidly.

The fat content of the liver may vary within wide limits and the amount present at any given time depends on many conditions. When there is an adequate intake of carbohydrate and of protein in the diet, the amount of fat found in the liver is almost constant. The fat content of the liver may reach 50 per cent of the total hepatic tissue in certain conditions. The fat content of the liver is increased when the diet is composed almost exclusively of fat; in the fasting state, in the presence of an available supply of fat in other fat depots of the body; in many pathologic conditions of the body, and following certain types of injury to the liver itself.

Manufacture of Food Materials.—Not all food substances, as absorbed from the intestine, can be utilized directly by the tissue cells or can be utilized as readily as when they are in another form to which they can be converted. The liver maintains its function of providing the tissues of the body with a constant supply of food by converting some of the substances absorbed in a nonusable form into one that can be burned by the tissues.

While the forms in which carbohydrate is absorbed are relatively simple, they cannot all be utilized directly by the tissues. Glucose appears to be the sugar of choice for utilization in the body. In all probability the carbohydrate that reaches the blood stream in other forms than glucose is converted by the liver into glucose or into glycogen.

Protein is absorbed from the intestine in the form of amino acids. Some of the amino acids absorbed are used to form new proteins for growth or repair of tissues or for storage. Since the body usually requires for these purposes only a part of the protein ingested, the remaining portion, which is often a considerable share of the total intake of protein, is burned for fuel. In order for protein to be utilized for fuel it is necessary for the amino acids to be deaminized. The nitrogenous portion is converted into urea for excretion as a waste product and the remaining portion is burned as carbohydrate. These two processes, deamination and formation of urea, depend on hepatic activity.

Knowledge of the processes of fat metabolism is very inadequate. The scanty evidence would indicate that the liver may be important in preparing fat for utilization by the tissues, as is indicated by the fact that in conditions of dearth of other foodstuffs, the fat content of the liver is increased.

Regulation of Food Materials.—It is not only essential that the body cells have a constant supply of food, but the amount of food which

reaches them must be regulated to meet their varying needs. In all probability hepatic activity is responsible for regulation of the more important supplies of food to the tissues, although the regulatory function of the liver has been demonstrated more clearly in regard to the control of the concentration of glucose in the blood. The concentration of glucose in the blood is one of the important physiologic constants. In order for the organism to function normally it is essential that the concentration of glucose in the blood be maintained constantly within rather narrow limits. These limits are different for various species of animals, but in almost every species they are very definite. When the concentration of glucose is above a certain limit, glycosuria occurs; if the amount of glucose is below the normal limit, symptoms of hypoglycemia occur. It is a vital function of the liver to maintain the concentration of glucose in the blood within definite limits. Not only is hepatic activity responsible for maintaining the normal values for the blood sugar, but the hyperglycemias are also dependent on the liver. The increases in blood sugar which occur following loss of the pancreas, injection of epinephrine, etherization, development of asphyxia, and so forth, do not occur in the absence of the liver. The mechanism whereby the liver accomplishes this regulation of the blood glucose is not known. There is some evidence that hepatic activity is important in controlling the supply of protein and fat to the tissues. The variable concentration of these two food substances in the liver is significant in this respect. It has been found that choline is an important agent in mobilizing the fat in the liver.

THE SECRETION OF BILE

The clinician usually has been more interested in the bile-secreting function of the liver than in the other physiologic activities of the organ. The secretion of bile was the first function of the liver to be recognized and that the condition of jaundice was associated with derangement of this function was known at the time when the total knowledge concerning the liver was scant.

The known facts concerning the secretion of bile can be stated briefly, but it must be recognized that there are many problems concerning this function of the liver which are not solved. Bile is formed by the hepatic cells and is passed into the canaliculi, which are the most minute portion of the biliary drainage system. Under normal conditions bile is secreted more or less continuously, but the rate of secretion, as well as the concentration of the various biliary constituents, varies greatly, depending on many factors, only a few of which are understood. Bile contains three main constituents: cholesterol, bile salts and bilirubin. The physiologic significance of the cholesterol found in the bile is not known. The bile salts are formed in the liver and under certain conditions may also be destroyed in the liver. The bilirubin is formed from hemoglobin in the reticulo-endothelial cells found in various tissues throughout the body. It has not been proven that the hepatic cells form bilirubin. Under normal conditions, bilirubin is excreted as a waste product. Bile has important functions in relation to digestion. It is one of the secretions which serve to dilute, buffer and neutralize the acidity of the gastric content which reaches the duodenum. The bile salts are necessary for normal digestion and absorption of fat. They also appear to be of special aid in the absorption of some of the vitamins and the deleterious effect of long-continued lack of bile in the intestinal content, such as occurs following formation of a biliary fistula, may be owing to the loss of this latter function.

THE DETOXICATING FUNCTION

Numerous substances that may be harmful reach the body by various routes. The gastrointestinal tract and other mucous surfaces are important portals of entry. Other injurious substances are formed within the body. Some of these are products of infection and others of deranged metabolism. The liver has been assumed to be the site where these harmful substances are destroyed. While it is undoubtedly true that the liver protects the body from many injurious substances, it must be admitted that it is difficult to prove that the liver converts a specific toxic substance to a nontoxic one and the number of substances which have been proven to be destroyed by the liver is not large.

Certain alkaloids, such as strychnine and nicotine, are for the most part destroyed in the liver. Other substances, such as epinephrine and ephedrine, are certainly not destroyed in the liver to any greater extent than in other tissues of the body. Many substances are made innocuous by conjugation, a process which appears to occur, to a large extent, in the liver. The liver may protect the body from toxic substances in other ways than by actual destruction. A large number of foreign substances which gain access to the body are excreted in the bile and, if they are not absorbed in the intestinal tract, can be eliminated by this means. There is some evi-

dence that the liver may absorb a toxic substance and hold it temporarily, releasing it in amounts too small to be injurious to other vulnerable sites of action. The view that the liver is important in protecting the body from many injurious substances is correct, but definite proofs in regard to specific substances and the manner in which they are made harmless are often lacking.

OTHER FUNCTIONS OF THE LIVER

The liver has many functions less understood than those mentioned. It appears to be concerned in some as yet unknown manner in the metabolism of water. Its large sinusoids offer the possibility for functioning as a site of storage for blood. It is probably the place of origin of the plasma proteins or of the substances from which these proteins originate. It appears to be an organ that is essential for some of the factors necessary for the coagulation of the blood; probably it is the site of origin of both the fibrinogen or its precursor, and of some of the prothrombin. The liver appears to elaborate certain specific substances, such as heparin, and to be the site of storage for other important substances, such as the factor essential in the treatment of anemia.

GENERAL CHARACTERISTICS OF THE LIVER IN RELATION TO PATHOLOGIC REACTIONS

In the liver take place several pathologic reactions which are characteristic for the organ. Some of these pathologic reactions in hepatic tissue depend on the peculiar type of blood supply to the liver; others, on the type of cellular constituents, and so forth. The most important factor in determining the character of some of the pathologic lesions of the liver is the great capacity of hepatic tissue to be restored after injury. The restoration of the liver after partial removal or injury is a most striking manifestation of the capacity of adult tissue to grow rapidly. After removal of approximately 70 per cent of the liver, the remnant of the organ will more than double in size in the course of the ensuing seventy-two hours and complete restoration of the total mass of hepatic tissue will occur within a few weeks. More than half of the hepatic lobules can be injured and exhibit central necrosis of a third of each injured lobule after administration of one of the hepatic poisons such as chloroform and yet, within two weeks' time, the organ will appear normal.

THE EXPERIMENTAL PRODUCTION OF PATHOLOGIC LESIONS OF THE LIVER

Numerous methods have been used experimentally to produce pathologic changes in the liver. The more important are the following: (1) obstruction of the biliary outflow; (2) diversion of the portal blood away from the liver; (3) infection, which usually has been brought about by changing the site of drainage of bile into the gastro-intestinal tract by such means as transplantation of the common bile duct or performing cholecystogastrostomy; (4) repeated administration of one of the hepatic poisons.

The resulting lesion, following any one of the methods mentioned, simulates some of the pathologic conditions found in the liver of the human being. The changes in hepatic tissue that follow obstruction of the biliary outflow in the animal are almost identical with those noted in the liver of man following obstruction of the common bile duct. The loss of the supply of portal blood to the liver is followed by atrophy which reduces the hepatic tissue to half, or less than half, of the normal amount. Drainage of the bile into the gastro-intestinal tract by an artificial opening is almost invariably followed by infection of the biliary tract and liver. This infection produces a cirrhosis, characterized by marked proliferation of connective tissue and continuous progression of the lesion until the hepatic tissue is destroyed. The repeated administration of carbon tetrachloride produces a cirrhosis which appears to be similar in all important respects to cirrhosis as it is seen in man.

THE REDUCTION OF HEPATIC TISSUE BY EXPERIMENTAL METHODS

The greatest obstacle to causing permanent decrease in hepatic tissue is the capacity of the liver for restoration. Three methods have been found whereby this ability of the liver to be restored can be injured. The portal blood supply appears necessary for the restoration of hepatic tissue; if the portal blood is diverted away from the liver, restoration after partial removal is greatly decreased. Obstruction to the biliary outflow or the repeated administration of an hepatic poison, such as carbon tetrachloride, also decreases or abolishes restoration of the organ. If any one of these three procedures is carried out and, at a suitable time subsequently, a portion of the organ is removed, restoration does not occur. It is thus possible to reduce the mass of hepatic tissue to only a small percentage of the normal amount.

RESUME

Certain facts have been learned, from experimental studies, of the functions of the liver and of the manner in which some of the pathologic lesions of the organ develop; some of these facts may be of clinical interest. While the results of studies on laboratory animals are subject to the justifiable objection that the reactions of the human being may not be the same as those of the animal, such results may be of value in suggesting problems for clinical investigation. In the ensuing few paragraphs, I wish to review briefly those of the facts learned by means of experimental studies which may be of clinical import.

Diet.—The results of experimental studies have indicated the importance of diet in relation to the functions of the liver, to the susceptibility or resistance of hepatic tissues to injury and to the maintenance of functions of the impaired liver. The liver has increased resistance to most forms of injury in the presence of a store of glycogen and usually is least resistant when the fat content of the organ is high. For instance, hepatic necrosis caused by chloroform occurs to a less extent in a glycogen-rich liver than when the glycogen content is low and recovery of the injured portions occurs more rapidly on a corbohydrate diet than on a diet of fat. A diet of fat increases the susceptibility of the liver to necrosis caused by carbon tetrachloride. The administration of alcohol in doses which are almost without effect on animals that are fed carbohydrate may be fatal to animals that are fed excessive amounts of fat. The survival time and general well-being of animals after complete occlusion of the common bile duct are markedly improved by a diet rich in carbohydrate. Animals of which the hepatic tissue is greatly reduced can be maintained in good condition for many months on a diet high in carbohydrate. The feeding of meat to such animals, even for a few days, often will prove fatal. Under certain experimental conditions, ascites can be made to come and go by changing the diet from carbohydrates to meat.

Cirrhosis.—Studies on the cirrhosis produced by carbon tetrachloride have been of value in indicating some of the factors responsible for this characteristic lesion. The administration of a sublethal dose of carbon tetrachloride produces acute necrosis of the liver. Recovery from such a lesion usually occurs promptly. If the drug is administered repeatedly, at intervals such that each dose is given before recovery from the preceding dose has occurred, marked cirrhosis of the organ is produced. It has been possible to follow the progression of the lesion and to determine the factors causing the characteristic features of the lesion.

The liver is completely invested with a thin covering of connective tissue which extends throughout the organ, forming a more or less complete wall around lobules and a supporting framework for the cords of hepatic cells. The arrangement of this supporting tissue is so definite, constant and characteristic in the normal organ that it presents an unvarying pattern to which changes attributable to pathologic processes in the organ can be compared. A study of the pattern of the liver during the process of development of cirrhosis owing to repeated administration of carbon tetrachloride reveals the following: After each repeated injury, restoration to some extent occurs, but restoration is not complete and the pattern of the liver becomes distorted. The most important defect in restoration is failure to establish the normal vascular relationship. As previously noted, restoration of hepatic tissue is dependent in a great measure on the portal supply of blood to the hepatic cells. The progressive failure of the establishment of the vascular supply within the lobule decreases more and more the capacity for restoration. As a portion of the lobule is repeatedly injured and restored, the supporting framework of each injured portion is pushed aside by the succeeding reparative process, thus producing a large portion of the increase in connective tissue which has given origin to the name of the condition.

Jaundice.—The accumulation of bile pigment in the tissues and blood is one of the most striking clinical signs of disease and usually indicates impairment of hepatic activity. The liver must be considered as an excretory organ for bilirubin because this pigment is produced chiefly extrahepatically. There may be many causes for failure of the liver to excrete bile pigment and to pass it into the intestine. The most common cause of jaundice is obstruction to the outflow of bile in some portion of the biliary tract. In this connection it should be noted that slight swelling of the hepatic cells, even the increase in size which accompanies the excessive accumulation of fat, may block the canaliculi and cause jaundice. The threshold of the hepatic

cells for excretion of bilirubin differs in the various species of animals. In some species, such as the dog, it is very low and the amount of bile pigment in the blood is very small. In other species, such as the horse and man, the threshold is sufficiently high for a measureable amount of bilirubin to be maintained in the blood. Changes in the character of the bilirubin, which make it difficult for excretion by the hepatic cells, may be a cause of jaundice. It should be noted that the liver alters the bilirubin that passes through it so that the bilirubin in the blood and in the bile are not quite the same.

Ascites.—Ascites may develop spontaneously in animals in which very extensive cirrhosis or obstructive jaundice of long duration exists. As previously mentioned, the ascitic fluid can be produced or removed by dietary measures. Animals which have obstructive jaundice or cirrhosis, or of which the hepatic tissue is greatly reduced, can be maintained in good condition and may give no evidence of ascites for many months. The substitution of meat for the carbohydrate diet almost invariably is followed by accumulation of fluid in the peritoneal cavity within a few days. The amount of ascitic fluid formed may equal 25 per cent of the animal's weight. The feeding of meat extract also will cause ascites to occur. Marked ascites may develop within four to six hours after as small an amount as 25 grams of meat extract has been given to a jaundiced animal or to one which has cirrhosis. The ascites usually disappears when the meat or meat extract is withdrawn from the diet and a diet of carbohydrate is reinstituted.

The mechanism of the development of ascites is not definitely understood. It is obvious that it does not depend wholly on impairment of the liver or on portal stasis. There are several pertinent problems in regard to ascites which are not solved. Among them are the following: What is the normal mechanism of circulation of peritoneal fluid? What parts do the parietal and visceral peritoneum, respectively, play in the formation of ascitic fluid? To what extent does the content of the intestine affect the accumulation of fluid in the peritoneal cavity? It appears highly probable that when appropriate conditions have been established, the ingestion of an irritant may be a frequent cause of ascites.

Diseases of Metabolism.—Since the liver has a necessary part in many of the processes of normal metabolism, it would appear justifiable to conclude that the organ is involved in many of the diseases of metabolism. The changes that occur in the liver after removal of the pancreas indicate that the liver is involved in diabetes. There appears to be an hepatic factor in other diseases of metabolism. In all probability it is rare that the hepatic factor is the primary cause of the disease, but rather that in many of the alterations of the processes of normal metabolism, hepatic activity responds to meet the changing needs of the body.

The Physiologic Activity of the Impaired Liver.—Studies on animals of which the hepatic tissue has been permanently reduced to only a small percentage of the normal amount have given some unpredictable results. It was found that many of the functions of the liver may be performed by only a small portion of the organ. Extensive injury, attended by a great decrease in amount of hepatic tissue, may have very little demonstrable effect on such functions as excretion of bile, regulation of blood sugar, deaminization of amino acids, formation of urea, and so forth. Certain other functions of the organ may be more easily affected; for instance, the formation of bile salts and the destruction of certain toxic substances. In general, it appears that, although total removal of the liver is uniformly followed by certain definite physiologic alterations, only a small amount of hepatic tissue is necessary to prevent such changes from occurring.

Liver Function Tests.—Several facts have been learned concerning the physiologic and pathologic reactions of the liver which are pertinent to a consideration of tests of hepatic function. It has been mentioned previously that the functional activity of the liver changes rapidly in rate and character and that most of the functions of the liver are but a part of physiologic processes involving many other tissues. Total removal of the liver causes several important physiologic processes to cease immediately and other processes are greatly modified. On the other hand, extreme reduction in hepatic parenchyma produces slight or no change in those physiologic processes which are so profoundly affected by removal of the organ. These facts are indicative of the difficulty of quantitating of tests of hepatic function and it would appear to be very fortunate that some of the tests are of no value clinically.

CERTAIN ASPECTS OF THE INTRACAPSULAR EXTRACTION OF CATARACTS IN THE AVERAGE PRACTICE*

REPORT OF FIFTY-EIGHT CONSECUTIVE CATARACT OPERATIONS

By RUSKIN G. ANDERSON, M.D.
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When glancing over the ophthalmological journals and papers of the past ten or fifteen years, one finds that intracapsular extraction of cataracts is the subject of a large percentage of these reports. There has been much controversy back and forth as to the merits of this type of operation for the extraction of a cataractous lens. The majority of these discussions have been presented by operators in the large clinics of the country and abroad, as they were first in position to form an opinion from the vast number of operations they perform each year. A very limited number of articles have appeared showing the results of extraction of cataracts in the capsule by ophthalmic surgeons with an average practice. I am therefore reporting on fifty-eight consecutive cataract operations that I have had an opportunity to do in the past two years. Many of these were clinic cases and did not return for refraction, so the final visual acuities cannot be given. The operative results were interesting and worthy of reporting.

Many inexperienced operators have been afraid to attempt the intracapsular extraction of the lens because they feel that it is a dangerous procedure for men with a limited number of operations to perform. The fear of getting away from the classic extracapsular or capsulotomy method of extraction of the lens is ever present. I agree that the beginner should do all in his power to master the orthodox procedure before attempting an intracapsular delivery of the lens. However, undoubtedly there are many selected cases in which the intracapsular extraction is an ideal operation, for example: the immature, nuclear or cortical cataract. In general, it may be said that in every case of senile cataract, intracapsular extraction may be attempted providing due caution is taken. Many excellent types of intracapsular extraction have been introduced since Colonel Smith delivered a lens in the capsule in 1895 by external pressure alone. His technic was to make a corneal section and without an iridectomy deliver the lens in capsule by exerting pressure with the heel of a strabismus hook over the cornea in its lower third, having a spoon placed above the upper edge of the corneal section for counter-pressure. This method has never been popularized in the United States and neither has the suction operation. The most popular method at the present time seems to be the forceps method either by the Knapp or Elschnig technic with various added modifications. These two men have done a great deal toward making the intracapsular operation an ideal method for the extraction of a cataractous lens.

Elschnig[1] has gone a step further and reported 136 cases of lens extraction in highly myopic eyes, by far the greater majority being done by his intracapsular method. He shows that the intracapsular extraction in highly myopic eyes is much superior to extracapsular extraction in respect to all complications. Knapp[2] says that the complication of the intracapsular operation which may be traced to the operative technic is a severe and definite form of iridocyclitis due to traction on the ciliary body. He gives an analysis of 500 successive cases. Beach and McAdams[3] contend that an operator is justified in attempting the intracapsular operation, providing he is successful with the classic method. They finally undertook the operation for patients with immature cataracts, since the intracapsular method has general approval for immature cataract extractions, and the result in 100 cases was so satisfactory that they have adopted the method as a routine practice. Experience persuaded them that the technic was suited not only to the requirements of the large clinic, but also to the operator with average opportunities. Appleman[4] prefers the Knapp method of extraction and thinks it should be generally used, as it is superior to the capsulotomy method, in his opinion. He reports the results of 300 intracapsular cases in his clinic at Wills Hospital and concluded that the intracapsular method gives a remarkably smooth and rapid recovery, with scarcely any reaction; that the patient requires but one operation; that the stay in the hospital is shorter and that the visual results are better. Gradle[5] compares the results of 200 consecutive extractions of cataracts, one-half by the Elschnig intracapsular method and one-half by the extracapsular method. He concludes that the Elschnig method of intracapsular extraction is just as safe in the hands of the experienced operator, if not more so, than the older capsulotomy method; the healing process is more rapid

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after intracapsular extraction; there is less irritation of the eye after intracapsular than after extracapsular extraction; and his percentage was markedly in favor of the intracapsular method in regard to secondary discissions and loss of vitreous. He had a prolapse of vitreous during nine extracapsular extractions among a hundred operations and only during three intracapsular extractions among a hundred operations. He thinks the ideal operation for removal of cataract today is the Elschnig intracapsular extraction with a round pupil.

Knapp[6] uses the Kalt capsule forceps for grasping the anterior capsule in its lower third. With the point of the Smith hook he makes counterpressure at the lower limbus backward and downward while the capsule forceps are carefully manipulated from side to side forward or upward; subluxation below usually takes place promptly. He then releases the capsule forceps and with the tip of the Smith hook pressing straight back at the lower limbus with counterpressure above against the scleral lip of the incision, the lens revolves forward or tumbles and the extraction is completed by sweeping the lens upward, thus separating its final upper attachment.

My method of intracapsular extraction is after the technic of Elschnig. A retrobulbar injection is made with procaine hydrochloride and epinephrine; a fixation suture is placed beneath the superior rectus muscle and a suture is placed in the conjunctival flap after a corneoscleral section has been made; a small peripheral iridectomy is made at the root of the iris and the lens extracted by a combined method of traction and external pressure. To do this, the capsule is grasped in its anterior lower third with a modified Arruga forceps and at the same time pressure is applied with the hook at the lower limbus. The lens is removed with tumbling, so that the inferior border is the first to pass through the incision. With one exception, the technic of the intracapsular and extracapsular extractions is quite similar. The essential difference is in the extraction of the lens after the incision has been made. If the lens capsule ruptures, the method may be changed to the old reliable extracapsular extraction. The lack of irritation of the eye during convalescence must be noted and is apparently due to there being no capsule nor cortex remaining to irritate the eye. This method of operation is well within the reach of any surgeon with average ability.

REPORT OF FIFTY-EIGHT CASES

Table 1
SEX INCIDENCE

	Extracapsular	Intracapsular
Males	19	28
Females	6	5

Table 2
AGE INCIDENCE

	Extracapsular	Intracapsular
Youngest	49 years	31 years
Oldest	80 years	77 years
Average	67 years	59 years

Table 3
TYPES OF CATARACT

	Extracapsular	Intracapsular
Immature	2	19
Mature	9	10
Hypermature	4	0
Diabetic	3	1
Complicated	7	3
Total	25	33

Table 4
TYPES OF IRIDECTOMY

	Extracapsular	Intracapsular
Preliminary	1	0
Complete	24	13
Peripheral	0	20
Total	25	33

The preceding tables are self-explanatory. Loss of vitreous occurred in five of the fifty-eight cases; three in the intracapsular operations and two in the extracapsular operations. Two of the three intracapsular losses of vitreous had complicated cataracts; however, one of the two extracapsular losses of vitreous had a complicated cataract also; so the type of operation probably did not play a great part in the loss of vitreous. I regret that I cannot give the final visual acuity in all of these cases, but in the ones that did return for refraction, the vision was better in the larger number of the intracapsular operations.

CONCLUSION

The intracapsular operation can be done by the ophthalmic surgeon with an average prac-

tice with very few complications during the operation when its technic has been mastered. Postoperative inflammation is lessened, hospital convalescence is shortened and discission is unnecessary unless an occasional capsule has ruptured. The intracapsular operation is ideal for the immature cataracts. The operative results of fifty-eight consecutive cataract cases are reported; twenty-five were operated by the extracapsular method and thirty-three by the intracapsular method.

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DISCUSSION (*Abstract*)

Dr. B. Y. Alvis, St. Louis, Mo.—The primary question here is not the intrinsic merit of intracapsular extraction, but whether this method is feasible and desirable in the average ophthalmic practice.

The answer depends on two aspects of the problem, namely, the merits of the method itself, and the possibility of the average eye surgeon's being able to employ it with as high a percentage of success as the simpler capsulotomy procedure.

As Dr. Anderson pointed out, recent literature contains many reports of large series of cases in the great clinics which show that the end results are somewhat better and the complications somewhat fewer than in the capsulotomy cases. Dr. Anderson's results also agree with this conclusion.

Having just heard a presentation of some of the practical and concrete evidence on the subject, it seems worth while to view the matter briefly in the abstract by thinking of an ideal cataract operation.

As an ideal end result there would be clear media, intact corneoscleral coat with circulation and drainage channels undisturbed, round active pupil, vitreous intact and protected by its diaphragm of zonule, and capsule with the ciliary body undamaged.

As to technic, this ideal procedure would be free from danger of complications due to faulty execution by the operator or to any action of the patient, and it would be free from postoperative risks.

There can of course be no ideal operation. The nearest approach is the perfectly executed linear extraction by the Barkan or similar method where all anterior capsule and all cortex are readily removed, the wound is small, self-closing and in non-vascular tissue.

Next to this is the simple extraction with removal of anterior capsule and all cortex.

In practice, however, we know it is possible to arrive at these ideal results in very few cases. Too often sticky cortex and capsular shreds remain to set up irritation and delay clearing of media. Too often anterior synechiae or iris prolapses ensue; while thickened capsules require frequent secondary operations.

Colonel Wright, in his "Lectures on Cataract," recently published, states that it took much longer for him to collect one hundred perfect capsulotomy operations than one hundred perfect intracapsular ones.

When the lens is removed in its intact capsule, the eye is at once freed of these troublesome and dangerous remnants. Also the added hazard of extensive irrigation of the anterior chamber is avoided. Finally, the end result approximates the ideal as to clearness of media; and if the operation is well executed and healing uneventful, the globe walls and uveal tract are practically intact.

The technic of the operation, however, does not possess the ideal simplicity and freedom from danger outlined above. The incision must be larger, approaching half the corneal circumference, thus rendering the eye vulnerable to slight misdirected pressure during and after operation. The rupture of the zonule and the delivery of the lens require a considerable degree of force that may expel vitreous or traumatize the ciliary body. The capsule and zonule may rupture as the vitreous face breaks, leaving behind a cortex and vitreous mixture in the anterior segment that may lead to an intractable phako-anaphylactic uveitis and shrinking of the eye.

Because of these added hazards, the average oculist rarely dared attempt intracapsular extractions until the great surgeons such as Knapp, Torok, Elschnig and others, taught us the safety measures necessary to offset them.

These safety measures are:

First, control the patient. Allay apprehension by sedatives and as little preoperative disturbance as possible.

Make the operation painless. Anesthesia is most important. Retrobulbar injection also reduces the tendency of the patient to move the eyeball inopportunely.

Preclude squeezing of the lids by complete akinesia of the orbicularis.

The bridle suture is valuable where for any reason the patient cannot be depended upon to cooperate perfectly.

Second, make the operative technic easy and safe. There must be room for the lens to escape. This means a large incision and a large pupil with iris flexible. If in doubt as to the ability of the lens to pass, make a complete iridectomy.

All pressure on the eye by lids or speculum must be avoided. Lid sutures for retraction are safer where the eyes are prominent. The assistant lifts lids and speculum away from the globe during and after delivery of the lens.

The final safety factor is the skill of the surgeon in balancing pull of the forceps on the capsule with the push of the lens hook on the limbus that comes from practice. This can be acquired by the use of animals' eyes and by doing the easy selected cases only by this method at first.

Those who have been doing eye surgery and are adept at extra-capsular extractions can readily adapt their technic to the intracapsular method.

Dr. Anderson has shown that the operation is entirely feasible for the well trained beginner. Dr. An-

derson is no longer a beginner, but when he came to us at the St. Louis City Hospital some years ago he was in search of experience. His first preceptors there were men who favored the intracapsular extraction and he soon became adept at it, as his results show.

Our custom in training resident eye surgeons at Washington University is to start them at extracapsular operations after six months as assistants in private surgery, where they see many cases of both types. When they have acquired the feel of the instruments and the ocular tissues, they may attempt intracapsular extractions. Most of them soon adopt this as their method of choice.

The delivery of the lens *in toto* has so many advantages, as shown by Dr. Anderson, in agreement with reports of large series of cases from clinics both here and abroad, that I would like to encourage every eye surgeon to master the technic by observing the operation by experienced operators and practicing it cautiously at first on easy selected cases, always employing the necessary safety devices emphasized above.

Dr. T. J. Dimitry, New Orleans, La.—I shall ask the privilege of showing a little instrument I use for the removal of the lens by vacuum grasping.

The instrument, though only the size of a comparatively large hypodermic syringe, will, when properly constructed, develop and control sufficient vacuum to remove the lens in its capsule.

You will note how well it grasps the skin of the forearm and how often it can be broken away and reapplied without again having to fill by the use of the plunger.

The plunger is worked by a spring which continues to make the necessary vacuum until the tensile strength of the spring is depleted.

This instrument is the one spoken of by Arruga in his conferences given recently in different cities and universities throughout the world.

A CLINICAL NOTE ON THE OCCURRENCE OF NEUROLOGIC MANIFESTATIONS IN INSULIN HYPOGLYCEMIA (SAKEL)*

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Recent advances in the treatment of the psychoses, especially of schizophrenia with Sakel's insulin hypoglycemia and von Medunna's metrazol therapy have justifiably attracted wide attention. Positive results with both methods have challenged the interests of investigators in the fields of neurology, metabolism and psychiatry, and a great many studies have been instituted. It is sufficient to mention in this regard that it has long been obvious that the reduction of blood sugar alone could not satisfactorily explain the changes in the psychotic process, nor the production of the visible neurologic changes. Evidence has already suggested that complex alterations occur in chemical constituents of the blood; in the physiologic activity of the entire endocrine system, and, as Cannon has shown, especially of the adrenals. There are in addition changes in the rate of oxidation of brain tissue, evidence that vitamins, especially C, and others are intimately involved somehow in brain tissue metabolism, and that the carbohydrate metabolism of nerve tissue is probably implicated. Even electric brain wave patterns are significantly altered after insulin and metrazol treatment of schizophrenia.

The alterations in the psychotic process have been interpreted by proponents of the various psychological schools in an attempt to fit the results into their own preconceived hypotheses. Regardless of the psychological school to which one may belong, we are all agreed that the acts of thinking, feeling, and behaving arise only in the presence of brain tissue. When these functions are restored to normality through the medium of preparations which produce objective evidence of marked central nervous system involvement during treatment, such neurologic manifestations take on primary significance.

Since schizophrenia, an incompletely understood psychotic process, is being altered by the relatively unknown mechanism of the insulin or metrazol therapy, it is clear that careful observations and investigation must precede even tentative explanations. Sakel and von Medunna have both justifiably been reticent in giving any hypotheses as to the mechanisms involved. The bewildering array of neurological manifestations observed during insulin hypoglycemia merit, therefore, detailed objective description, as a first step in the study of this very complex problem.

While the symptoms arising in accidental hypoglycemia during diabetic treatment or in pancreatic adenomata are well known, the descriptions have not often been concerned with the neurological patterns to be seen in deep hypoglycemia. Occasionally, when severe neurologic complications did appear, they were reported in the nature of a curiosity. Miller and Trescher, for example, reported such an instance in which amnesia, epileptiform convulsions and hemiparesis occurred. In so far as I can determine detailed studies of neurologic changes appearing in deep prolonged hypoglycemia, such as that

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used in the method of Sakel, have not appeared in our literature.

In a recent publication I described in some detail the clinical appearance of the neurologic manifestations occurring in Sakel's hypoglycemic therapy. These neurologic occurrences were observed on the insulin wards of the Harlem Valley State Hospital, where the treatment had been instituted with the help of Dr. Sakel himself. They were arbitrarily divided into prolonged and sudden manifestations.

(1) Prolonged manifestations were those occurring for a longer period during the four to five hours of treatment.

(2) Sudden manifestations were those which occurred suddenly and usually toward the end of the treatment.

(1) The prolonged manifestations occurred as follows: Soon after the insulin had been given the patient ordinarily remained quiet and resting. During the second hour, when diaphoresis was usually well established, there would ensue either somnolence, restlessness, mild excitement or shouting. This usually passed off as the hypoglemic state progressed into deeper coma. In this phase one could observe:

(a) Quick, jerking movements of the arms, legs, body and restless tossing of the head. A sudden flexion, but less frequently extension of both arms was extremely common. These movements often recurred for an hour or more during the treatment and as often as 15 to 20 times per minute, although the rate varied greatly. Touching or shaking the patient frequently initiated such flexor arm jerks.

(b) Some patients exhibited prolonged sucking movements of the lips. No special emotion could be noted in the facial expression during these movements. At times, there was marked grimacing of the face accompanied by bilateral athetoid movements of the extremities.

(c) There were episodes initiated by flushing of the face, dilatation of the pupils and labored breathing. These were associated with rigid extension of the lower extremities, bilateral adduction and extreme internal rotation of rigidly held arms. Their wrists were rotated to hold the palms outward. The fingers were most often tightly clenched into the palm with the thumb projecting characteristically between the index and middle finger, or the ring and middle finger. The eyelids were often retracted widely, producing a picture of extreme fright. The whole movement was slow and rhythmic. After about thirty seconds to one minute the arms and legs would relax and resume a neutral position until the next movement began again. This picture at its height clinically suggested the attitude of decerebrate rigidity.

(d) There occurred also a partial manifestation of the above. The arms would rotate, the palms face outward, but the limbs would remain fairly well relaxed and this position would be maintained for long periods without interruption.

(e) Irregular, thrashing, apparently purposeless movements of the arms and legs were frequently noted. At times there seemed to be definite attempts to brush away the physician's arm or the towel on the patient's forehead. These movements suggested true defensive movements. The patient often struck the bed, the wall, or his own face during this activity.

(f) The deep reflexes were difficult to evaluate because of the constant spasm in the extremities which interfered with their elicitation. However, following the somnolent stage, the Babinski reflex would appear and then become sluggish as the patient approached deeper coma. The corneal reflex also disappeared in the later stages of coma. More often the Babinski appeared as part of a general flexor withdrawal reflex, but toward the deeper stages of coma it could be elicited alone before its final disappearance in deepest hypoglycemia. Its appearance or disappearance apparently mirrored the depth of the hypoglycemic shock.

(g) Slow, trombone-like movements and irregular jerks of the tongue often were seen. A spontaneous clonus of the lower jaw and clonic movements of the upper eyelids sometimes appeared for a short while.

(h) The extremities often assumed a posture resembling that seen during the movements of dystonia musculorum or athetosis; however, they remained fixed in these positions, suggesting the term, frozen athetoid movements, for their description. Dr. Dussik told me of seeing true hemi-ballistic movements as well as athetoid position of the hands in his Vienna material.

(i) Transitory hemiplegia also occurred. Drs. Cline and Schwoerer told me of seeing a hemiplegia which lasted for nine hours. I observed several transitory hemiplegic states. In one instance, a case on Dr. Goulacher and Dr. Pellens' service showed a transitory palsy of the left side of the face which preceded an epileptic seizure.

(j) One could frequently elicit the grasp phenomenon. Groping was never manifested and this again proves the contention of F. M. R.

Walshe and E. Graeme Robertson that groping occurs as part of the grasp phenomenon only if the patient is conscious or can see the examiner's hand and, therefore, is not involuntary as is the grasping.

(2) Sudden neurologic manifestations were as follows:

(a) Convulsive seizures frequently occurred and could be clearly distinguished from the other convulsive movements of a more prolonged character in most instances. It was often difficult for me to decide exactly when a series of convulsive movements could be grouped as a seizure. The definition of what constitutes a true epileptic seizure is still highly unsatisfactory. Certainly if we call mild disturbances of consciousness with slight twitching a *petit mal* attack in everyday medicine, it then becomes quite difficult to state that a series of severe convulsive movements in an unconscious patient is not a true epileptic seizure. Sakel himself uses the term in a rather indefinite way and so do most of us.

(b) In about a dozen instances there occurred a sudden dramatic complication usually toward the end of treatment. One of these I witnessed. These alarming manifestations were particularly frightening to the onlooker when seen for the first time. The staff felt that this particular complication, to be described, may represent a specific type with special prognostic features. Dr. Dussik stated that in his experience it had occurred only about five times in several thousand treatments. It usually developed as follows: when the regular proceedings for the termination of the hypoglycemic state had been instituted the patient would fail to regain consciousness. By previous experience the doctors had found that if such a patient did not react in forty-five minutes in spite of intravenous glucose, trouble was in all probability to be expected. The patient at this time was noted to have constricted pupils, which then slowly dilated and were associated with marked flushing of the face. There then ensued an excited phase with convulsive movements, contortions, rigid attitudes and extremely labored breathing, this phase lasting from fifteen to twenty minutes. It was so severe that the patient appeared to be *in extremis* and completely exhausted. The movements would then slowly subside in severity and duration, the pupils return to more normal size, and the patient relax in complete exhaustion with shallow rather slow respirations. After a lapse of ten to twenty minutes, another phase would begin, augment to a frenzy of labored, irregular movements and again subside. These alternating periods of activity and relaxation at times continued for one to two hours, diminishing, however, in duration and severity with each attack. It seemed as if the whole central nervous system was thrown into a frenzy of disorganized activity. The general impression was that an overactive, totally disorganized central nervous system was being thrown into activity, and suggested to me the term neuro-physiologic crisis. In this complication and throughout the hypoglycemic state there were recognizable hemiplegic attitudes, extrapyramidal manifestations of transitory cog-wheel rigidity, and signs of mid-brain involvement in the disturbed extra-ocular movements, the eyeballs moving asynchronously. There were also signs suggestive of disordered thalamic or medullary control of temperature, pulse and respiration which appeared entirely dissociated from their usual relationships. For example, the temperature being 104.2° F., the pulse was one hundred and sixty and the respirations as high as eighty per minute in one instance. There were in addition manifestations of overactivity at the lower levels of the brain stem as judged by the occurrence of opisthotonus and the attitudes of decerebrate rigidity. There also occurred overactivity of the autonomic nervous system: the dilatation of the pupils, flushing of the face and rapid pulse, suggesting sympathetic overactivity; the contraction of the pupils and pallor, parasympathetic overactivity. It was extremely difficult to separate the rapidly changing pictures and fit them into neurological schemes. All the movements and postures just described were most often bilateral, but at times unilateral. In spite of their severity they were reversible in character and the patient awoke from his hypoglycemic coma, if uncomplicated, with no trace of the neurologic storm through which he had passed. Following the severe complications, however, where the patient failed to arouse, his final awakening after many hours would still be characterized by evidence of mental confusion which could last for several days and at times as long as two or three weeks.

The staff has made the interesting observation that patients who experienced this severe complication usually emerged from their confused after-state with definite signs of progressive improvement. From a clinical neurologic point of view we see a bewildering array of neurologic patterns. On closer study we recognize that we are really witnessing a reversible type

of dissolution of the nervous system in the sense of Hughlings Jackson, in which the higher cortical centers are shunted out and the patterns become characteristic of lower and phylogenetically older mechanisms in which we see a similarity to known clinical conditions as they appear in man with disease of the basal ganglia and lower brain stem.

In some of the movements, such as grasping and sucking, we see phylogenetically old patterns. Bieber has shown that grasping is easily elicited in the new born when they are awake, or sucking, especially when tension is made on the upper limb. Apparently grasping is observed to be in relation to mechanisms for support and to the function of sucking or eating. This sucking and grasping is most pronounced before a feeding, and after the infant has nursed these cannot be elicited. Grasping and sucking are probably the first and basic functions of the hand and mouth. They appear pathologically in adults, alone or combined, when there is disintegration of the nervous system. Grasping may occur in association with its equivalent mouth-opening. The more complete the disorganization, the more nearly does the adult sucking approximate its basic infantile level. It has often been observed in general paralysis, alcoholism and encephalitis, especially where the disturbance involves the extreme frontal areas, or corpus callosum, areas important in the organization of activity.

When we consider the essentials of camphor and metrazol treatment we again see that a reversible disorganization of the nervous system plays the visible role in the treatment. In a recent preliminary report by Drs. Watters, Goldsmith and myself, we described the convulsive seizures after metrazol and compared them with those seen in other clinics where metrazol is being used. While the seizure itself was too rapid to disclose any phylogenetically older patterns of activity, even if they were present, it is interesting to note that wide opening of the mouth frequently initiates the seizure, and that following the convulsion sucking and chewing movements are frequently included among other automatic activities.

The prognostic significance of the epileptic seizure itself, even in insulin therapy, has changed somewhat. Originally Sakel cautioned workers to terminate the epileptic seizure at once. He has recently evinced the belief that it may actually be beneficial and in his letters to von Medunna, which I was privileged to see, he denied that he ever considered them undesirable. Epileptic seizures occurred in about a third of the insulin treated cases in their country, and the same number occurred in Max Müller's report on his material in Switzerland. As a matter of practical fact, the seizures were always over by the time intravenous glucose administration was begun, so that the patient usually completed the seizure anyway. It is interesting to note that Friedman did not advocate terminating seizures occurring with camphor until after six had occurred one after the other.

We are still in a period of objective description and careful evaluation in regard to both the insulin and metrazol treatments. It is encouraging that numerous investigations have been launched, some completed, and many others continue. My own observations and interpretations cover mainly what I have seen and are oriented by the views of Hughlings Jackson. It is interesting to note that Dr. Smith Ely Jelliffe, in looking at this therapy from the standpoint of the analyst, says nearly the same thing when he states that "by the hypoglycemic threat we can envisage a type of phylogenetic dissection by a metabolic tool from frontal forebrain back to the medullary respiratory and vagus nuclei, and a decerebration experiment of a very subtle form by a pharmaco-dynamic type of instrumentation."

A great deal of work must still be done. We hope that future study and evaluation of both the insulin and metrazol therapies will disclose facts which may help us to understand these unusual neurologic states, and the psychotic processes and mechanisms involved. Until then we are forced to be content with close observation and careful reporting of data.*

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HISTORICAL CONSIDERATIONS OF PUERPERAL SEPSIS*

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The history of puerperal sepsis begins in the fifth century B. C., in the writings of Hippocrates. Hippocrates has been called "Father of Midwifery," as well as medicine. In his writings on the diseases of women he has given a description of a case of puerperal sepsis which is here quoted from an essay by Dr. C. H. Peckham:[1]

"If, however, the purgation of the puerperium does not take place, the next thing is likely to be a fever with a chill, while the abdomen becomes swollen. If you touch the patient the whole body feels the pain of it, and especially if anyone should touch the abdomen. At the same time also a burning sensation in the abdomen is noted and there are apt to be pains in the loins. The patient's appetite becomes fastidious, and wakefulness and irritability occur. After this, on the fifth or seventh day, there may be an evacuation of the bowels, and the material passed is black and is sometimes of a very bad odor. The urine is not unlike that of an ass. If this movement of the bowels takes place it appears better for the patient, and with proper treatment she may be restored to health. The arterial pulse is always weak, at times also quick, more rarely strong, but thin. This occurs at the beginning of the disease and is apt to continue. Fomentations should be applied to the external genitals made of sweet smelling herbs, which, if applied every day, will bring about an improvement of the conditions. If, however, the matter that should be purged after the puerperium be carried forcibly to the head or to the thorax and lungs, which sometimes happens, death may rapidly take place if it is detained there."

In the second century A. D., Soranus of Ephesus prepared the first medical treatise which dealt exclusively with diseases of women. In the chapter on puerperal fever, the beliefs of Hippocrates were upheld, but nothing new was added. However, the works of Soranus served as the original for the famous "Rosengarten of Roslin." In 1513 the book was translated into English under the title of "The Byrth of Mankynde," by Thomas Raynalde. It was the first book on midwifery to appear in the English language. This book contained a paragraph under the description of puerperal infection and instructions for the fever. The treatment consisted mainly in giving a concentration of herbs, purgation and fomentation to the abdomen which was thought to aid in a free drainage locally. Venesection was also recommended.

*Chairman's Address, Section on Obstetrics, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

In 1570, Mercatus made the statement that puerperal fever developed from a putrefaction of lochia retained in the uterus. He later stated that the illnesses of puerperal women were caused by an inflammation of the womb which was due to a difficult labor.

A very good paragraph on the cause of puerperal fever was written by Felix Plater, who, in 1602, said:

"First of all, because of the difficulty of labor, the great pain and effort involved, the uterus frequently becomes inflamed. Then, either because the foetus or some of the secundines remain, or even after these have been expelled, pain and fever may assert themselves because of the inflammation that had begun before their expulsion. The retention of the secundines alone would not affect them so rapidly as this inflammation, which is likely to follow, and which constitutes the chief cause of death except in those cases in which there is a large loss of blood."

In 1612, the second textbook on midwifery in the English language was published with still no reference to puerperal infections. Around 1640, Sennert stated, "that a depraved condition of the blood was frequently the cause of puerperal infections." We do not know whether he was considering an anemia when he used the words "depraved condition."

A very great contribution to the etiology of puerperal infection and one which gives us a somewhat modern view of the changes within the uterus, was given us by William Harvey in 1651:

"A foul and putrid lochia sets up fever and other violent symptoms. Because the uterus, torn and injured by the separation of the placenta, especially if any violence has been used, resembles a vast internal ulcer, and is purified and cleansed by the free discharge of the lochia. Therefore, do we conclude as to the favorable or unfavorable state of the puerperal woman from the character of these excretions. For if any part of the placenta adhere to the uterus, the lochial discharge becomes fetid, green, and putrid; and sometimes the powers of the uterus are so reduced that gangrene is the result, and the woman is destroyed."

In the middle of the seventeenth century, puerperal fever occurred in epidemics, the first one in Leipsig. More than two hundred epidemics occurred during the next two hundred years, according to Burtenshaw. It has been said that during the first epidemic, one in about ten persons escaped death.

The third English textbook on midwifery was called "The Childbearer's Cabinet," in 1653, and yet no mention was made of puerperal sepsis. In 1668, a French obstetrician, Mauriceau, was the first author to describe peritonitis following the sepsis of childbirth, and is here quoted:

"This sudden suppression of the lochia, the matter of which choking up, as it were, the whole substance of the uterus, and there stagnating, causes a great distention of the part, and an inflammation, which communicated itself, by means of the peritoneum, to the whole hypogastric region; which hence becomes inflated, distended, and extremely hard, and if the complaint is not soon removed, it frequently proves fatal in a very short time."

In 1686, Puzos was the first man to give a clear account of "milk fever," about which he said:

"Milk, circulating in the blood, is attracted to the uterus during pregnancy and to the breasts after confinement, but metastases might form in other parts and produce the symptoms of malignant or intermittent fever."

In 1709, Boerhaave seems to have been the first man to advise against bleeding or venesection in this disease.

Edward Strother, in 1716, published a book called "Criticon Febrium or a Critical Essay on Fevers." He seems to have been the first to point the way towards modern concepts of puerperal fever and was the first to use the term.

Mead, in 1742, described conditions in the findings of an autopsy of a puerperal sepsis. "He found that in many cases the uterus was macroscopically healthy in appearance." This is true today, particularly in some of the acute streptococcic infections.

In 1751, John Burton was the first author to suggest that a puerperal infection might be transferred to a patient by an outside agent and he stated that, "inflammation of the uterus during the puerperium might be caused either by a suffusion of the lochia or by the carelessness of the midwife or of others attending the delivery."

John Leake,[2] of London, published an article, "Observations on Childbed Fever," in 1772. He was among the first to suggest the infectious and contagious nature of puerperal sepsis. He wrote a paragraph which gives the views of that time:

"The childbed fever, when by a distemperatic of the air, like the epidemical dysentery or ulcerous sore throat, may at last become infectious; but when it only arises from such accidental causes as have already been enumerated, and which are confined to particular habits and constitutions, I believe it will then never communicate itself to a second person."

Alexander Hamilton, in 1871, seems to have been the first author to state positively:

"The childbed fever is remarkably contagious, and when epidemic, capable of being propagated from one person in the puerperal state to another."

Baudelocque suggested in 1789 that puerperal infections could be produced by the introduction of the hand and instruments into the parturient canal. This statement probably is the first suggestion on the prophylaxis of puerperal fever. A notable work was performed by Dr. Joseph Clarke, when he handled his patients during an epidemic of puerperal sepsis. In Dublin, in 1790, he recommended isolation of all infected patients, thorough washing of linens and mattresses, repainting of walls, floors and beds. It was his belief that the nature of the condition "rendered it probable that this fever derived its origin from local contagion, and not from anything noxious in the atmosphere. So the wards where the infection had occurred were closed and the epidemic ceased."

John Clarke, in 1793, also wrote:

"Accidental violence offered to the parts concerned in parturition will also sometimes lay the foundation of a fever, such as stimulating the os uteri, either by too frequent examinations or by attempts to dilate it. Violence offered by the improper use of instruments may become a cause of fever. The hasty delivery (manual) of the placenta immediately after the birth of the child can never be necessary, except in cases of hemorrhage, and must endanger the life of the woman in many cases."

We are prone to attribute to Holmes and Semmelweiss the honor of definite statements in the contagiousness and infectiousness of puerperal sepsis, yet Alexander Gordon, in 1795, fifty years ahead of Holmes, wrote in his treatise on the epidemic of puerperal fever:

"That the cause of this disease was a specific contagion or infection, I have unquestionable proof. This disease seized such women only as were visited, or delivered, by a practitioner, or taken care of by a nurse, who had previously attended patients affected with the disease. Every person who had been with a patient in the puerperal fever became charged with an atmosphere of infection, which was communicated to every pregnant woman who happened to come within its sphere. It is a disagreeable declaration for me to mention, that I myself was the means of carrying the infection to a great number of women."

"To prevent all this, he recommended the burning of bed clothes and the apparel of the infected patient, thorough washing of the apparel of the attending doctors and nurses, with the fumigation of their apparel."

In 1815, David Hosack of New York, the first American physician to write on the subject of puerperal sepsis, said:

"Puerperal fever is not infrequently highly contagious."

In 1819, Labarraque "made the first chlorine solution for disinfecting purposes," which seems to have greatly aided the doctors of that time. In the same year William Street recommended the sterilization of instruments and materials by dry heat. The commission of Health of Marseilles in 1825 published a bulletin containing these instructions:

"The physician, almoners, servants, and all those who take care of the sick, before approaching them, and on quitting them (are) to wash their hands with chlorureted water."

In 1827, Alcock published an article on the medical use of chlorurets. These statements marked the beginning of surgical disinfection and sterilization as a part of modern obstetrical technic. In 1831, Robert Lee wrote on "Uterine Inflammation in Puerperal Women," "published the results of careful autopsy studies, and distinguished definitely the terms of peritonitis, parametritis, metritis, and thrombophlebitis." From Edinburgh, in 1822, William Campbell wrote:

"During parturition we should avoid frequent examination and we ought on no account to interfere unnecessarily either for our own accommodation in consequence of the pressure of business or to please the impatience of the female herself, or her attendants."

In 1835, "Robert Collins wrote of the experience of the Rotunda Hospital in Dublin where 10,785 women had been delivered without a single death from infection, subsequent to the establishment of a routine of thorough cleanliness and disinfection of wards, beds, and so on, together with the cleaning of equipment with chlorine water." In 1834, Oliver Wendell Holmes[3] published "Puerperal Fever as a Private Pestilence." Among American physicians he stirred up a great deal of controversy and helped to crystallize the means and the ideas for preventing puerperal sepsis.

In 1847, "Semmelweiss was an assistant in the first obstetrical service of the Allgemeines Krankenhaus in Vienna, had been present at the autopsy of his colleague, Koletschka, who had died of septicemia from a cut sustained in an autopsy." Semmelweiss says:

"In the excited condition in which I then was, it rushed to my mind with irresistible clearness that the disease from which Koletschka had died was identical with that from which I had seen so many hundreds of lying-in women die. The puerperae also died from phlebitis, lymphangitis, peritonitis, pleuritis, and meningitis, and in them also metastases sometimes occurred."

"Moreover, he noted that his own ward, with a very high mortality, was used by students coming directly from the dissecting room, whereas the second ward, with a much lower death rate, was given over to the instruction of midwives who had no such contacts. He further noted a cadaveric odor on the hands of the students and hence:"

"In order to destroy the cadaveric material which adheres to the hands, I began about the middle of May, 1847, to employ chlorinated liquids, with which every student was required to wash his hands before making an examination. Later a solution of chlorinated lime was substituted because it was not so expensive."

"All seemed to justify the conviction that the hitherto unknown endemic cause of the frightful devastation which puerperal fever had wrought in the first clinic had at last been discovered; it was simply the cadaveric material adhering to the examining hands in the first clinic." The writings of Semmelweiss stirred up a great controversy in Europe as did those of Holmes in America.

The next advances to be made in the study of puerperal sepsis seems to have been in referring the etiology to bacterial agents. Rokitansky, in 1864, found germs in the lochia of cases of puerperal fever which, injected into the bodies of experimental animals, produced abscesses. The next year Mayerhofer observed that micrococci could be found in the tissues of various organs of women who had died from puerperal fever.

Coze and Felz, in 1868, found for the first time streptococci in the blood of a woman dying of puerperal sepsis. A few years later, about 1880, Pasteur succeeded in obtaining pure cultures of streptococcus from the blood of a case of infection. It was thought for a long time that "the only bacterium capable of giving rise to puerperal fever was the hemolytic streptococcus." This was assumed by Schottmuller. Later Schottmuller taught that:

"All puerperal fevers are caused by an invasion of bacteria into the blood stream in varying amounts and varying intervals."

This is probably one of the soundest doctrines in puerperal sepsis and led to the formulation of this guiding principle:

"The location of the septic focus, the depth and extent of the bacterial invasion and the frequency with which pathogenic bacteria gain entry into the blood stream, are by far more decisive factors in the prognosis and the treatment of puerperal sepsis than are the labo-

ratory determinations of bacterial virulence, or the pathologic study of bacterial penetrability."

In the study of puerperal infection, first, "bacteriologic examinations of secretions of the vagina and cervix and the blood should be made; second, bimanual palpation of the uterus, the adnexa and the parametria should be done; third, temperature curves should be studied. Fourth in importance is a general check on the patient's resistance to determine if possible, whether the infection is autogenous."

Schottmuller was in favor of a bimanual examination at the beginning of puerperal infection. "Every bacterial infection," he said, "is accompanied by an intoxication; their association is inevitable. To combat the latter we must eliminate the former." Schottmuller was of the opinion that "as long as the endometrium alone constituted the septic focus, the accompanying streptococcus bacteremia was practically harmless." On the other hand, if the "parametrial lymphatics" became involved, the mortality in puerperal infection rose to 50 per cent; if the pelvic veins were involved, the mortality of 90 pen cent ensued; and when the endocardium became infected the mortality became 100 per cent.[4]

Auto-infection was proven by Ahlfelf in 1897. Aschoff (from M. R. Robinson[5]), in 1911, classified puerperal auto-infection into endogenous, ectogenous and exogenous. "From an academic and formative point of view, these classifications are important." "It would, however, serve the welfare of our patients best if we were to lock this knowledge in a subconscious compartment of our brain and never let it come to the surface of our medical consciousness and thus maintain an eternal vigilance on sepsis."

I am much indebted, in the writing of this paper, to the essay "A Brief History of Puerperal Infection," by Dr. E. H. Peckham,[1] and also to the paper, "Revaluation of the Prevailing Theories and Principles of Puerperal Infections," by Dr. M. R. Robinson.[5] I have quoted frequently from their papers as well as their quotations.

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THE APPRAISAL OF MEDICAL SCHOOLS*

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The principal business of the Council on Medical Education and Hospitals of the American Medical Association is the appraisal of medical schools. Some of you perhaps have already asked yourselves, why should there be a voluntary organization, like the American Medical Association, concerning itself with the evaluation of medical teaching in the United States? In order to understand the answer to that question, it will be worth while for just a moment to briefly review the history of medicine in the United States.

During the Colonial period, as you can well understand, educational institutions of all sorts in this country were on a very low level. They were undeveloped. The institutions which called themselves colleges were for the most part, designed to train men for the Christian ministry. Men who wanted to practice medicine were forced to choose one of two alternatives. If they were financially well off and very ambitious, they would go to Europe and study medicine, very often to Edinburgh, because at that time it was the best developed medical teaching center in Great Britain.

If they could not go to Europe to study, they had to resort to the apprenticeship method of learning their profession. They would apprentice themselves to a physician and for a period of three, four or five years, they would assist him in his practice. They had to look after his horse and wash his buggy, and probably milk the cows, and go out with him on expeditions into the woods to gather herbs and plants from which he made his remedies. They would drive around with him through the country if there were roads, or ride behind him on a horse if he had to travel horseback and, little by little, as they became more familiar with the work of the physician, they would be brought into the houses of the patients and permitted to watch the physician while he examined them and treated them and, as they showed a sufficient interest and proficiency, they would be allowed to assist the physician to a greater degree and ultimately to han-

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dle some of the patients themselves; then they would start out to practice for themselves.

This apprenticeship method, which was in vogue not only in the professions but in the crafts, had a great deal to recommend it, but as the science of medicine developed, as more and more began to be learned about anatomy and physiology, and especially about pathology, it was realized that this method of teaching was entirely inadequate; that a great deal depended upon the quality and the qualifications of the preceptor, and upon the situation—where he happened to be, the character of his environment and kind of patients he would receive. A man who lived in one section of the country might learn a great deal about malaria, and a man who lived in another section about pneumonia, but there was no possibility of arranging the selection and the variety of the cases that were studied in such a way as to meet the student's need for a broad understanding of all phases of medical practice.

So just after the period of the Revolution an effort was made in Philadelphia to establish in this country a medical school patterned somewhat crudely after the University of Edinburgh, the idea being to bring students together for at least a part of their period of training and give to a group of men a course of systematic lectures designed to meet their needs, to fill in the gaps of their own personal experience, and to render them more all around and more thoroughly trained physicians.

The first attempt to regulate the practice of medicine in this country, of which I know, was made in New York State in 1766. That was just prior to the Revolution, and a law was passed by the Provincial Assembly in Albany that no man might be permitted to practice medicine unless he had passed an examination conducted by a board of three persons consisting of the Lieutenant-Governor of the Province, a judge, and an Army officer selected by him. The preamble states that because of the growth of quackery as practiced by incompetent and unskilled persons, it was necessary to do something to regulate the practice of medicine and to protect the public interest.

It is of great importance and of interest to us to recall the preamble to that law, which was passed more than 150 years ago, because it expresses exactly the grounds on which all legislation regulating the practice of medicine since that time has been based. It was designed not in the interest of the medical profession, nor to protect those who were in practice, but to protect the people from the evil consequences of ignorance and incompetence at the hands of untrained persons who assumed the responsibility of dealing with the sick.

The first medical school, as I told you, was started in Philadelphia at the very end of the Eighteenth Century, and in the early years of the Nineteenth Century a few more medical schools were started, but there was not any very great increase in the number of medical schools until after the middle of the last century.

In the meantime, a change had taken place in the method of regulating the practice of medicine. After the Revolutionary War, when our states were formed, some of the early ones began to attempt to establish a systematic basis for determining who might and who might not practice medicine. Whether it was at the solicitation of the medical societies or not, I cannot say, but the fact was that the medical societies were given the privilege of deciding who might practice. The idea seems rather strange to us today, because we have been brought up in another generation when the right of decision is supposed to rest entirely with the officials of the state. Yet the arrangement is not so strange as it might seem because for many years the bar associations were entitled to determine who might practice law, and in some states the courts still exercise that power.

In the early part of the last century most of the states that had any laws governing the practice of medicine permitted the state medical societies to determine the fitness of applicants. That would not have been so unsatisfactory if it had not been for one circumstance, which was entirely accidental but was profound in its influence, and that was that in the early part of the last century there was launched in Germany a new system of the practice of medicine called homeopathy. You all know something about the founder, Hahnemann, and his idea that all diseases could be cured by administering minute doses of some drug which, in larger doses, would produce exactly the symptoms from which the patient was suffering. There was no foundation in fact for the theory underlying homeopathy, but neither was there any basis for rational therapeutics at that time. All medical treatment was based on empiricism, some of it very crude, and the fact that the patients of homeopathic physicians got well as fast as the patients of other physicians who were receiving large doses of medicine made homeopathy very popular. Subsequently the establishment of homeopathic medical societies gave them an equal

right with other societies to determine the eligibility of the practitioners of medicine.

When, a little bit later, it became necessary to take the control of medical practice from the medical societies and put it into the hands of state officials, the people were already so thoroughly accustomed to the idea that there were two kinds of medical practice, just as we have a great variety of denominations in the religious field, they could see no alternative than the setting up of two entirely independent boards of medical examiners, homeopathic and regular, for the licensing of physicians.

About the same time, that is, after the Civil War, the number of medical schools in the country began to increase with great rapidity. This was due partly to the extension of the population into the Western areas, the rapid growth of the population through immigration, and the settlement of large areas where physicians were few and an attempt on the part of the citizens to supply the immediate needs of those communities by turning out physicians rapidly from among their own numbers.

Thus it came about that in many parts of the country a group of half a dozen doctors would get together, hire a hall, put in a stove and blackboard, and call it a medical school. That was all they needed, and students flocked to them. The fees they paid were not very high, but whatever they were they were divided among the members of the faculty at the end of the year. The most important benefit which these teachers derived from their connection with the medical school was the fact that they were highly regarded by their students who, when they got in trouble in their practice, were likely to call on their former preceptors for advice. The preceptor profited by the consultation fee, and gained a greater reputation in the community.

There followed a period during which the number of medical schools was rapidly increasing, and the character of the instruction given in the medical schools was not so good as the instruction that had been given in the older days under the apprenticeship system, because under the latter system the student at least saw patients, knew them personally, felt their pulse, looked at their tongues, took their temperature, bathed them, and gave them stupes, enemas, or poultices. He knew what sick people were like and what had to be done for them according to the knowledge prevailing at that time. When there was substituted for the apprenticeship system the method of gathering students together for a short period and lecturing to them, without any practical experience whatsoever, it was a step backward in the development of medical education in this country.

It was about that time, the last quarter of the last century, when the states began to realize that they must take from the medical societies the responsibilities for licensing physicians, and during a period of about twenty-five years nearly all of the states passed laws forbidding anyone to practice medicine except those who had received a license from the state.

In order to determine who were qualified to receive a license, boards of medical examiners were appointed to conduct an examination as to the fitness of the candidates who appeared before them. Logically and theoretically, this was all right. It was actually what should have taken place at an earlier date instead of placing the control of medical practice in the hands of the state societies.

Fundamental difficulties soon appeared. The state boards of examiners were politically appointed. They received no salaries. They were permitted only to divide among themselves the examination fees they might receive, which for the most part were meager and not sufficient to provide them with proper organization to do their work. Very often, the personnel of the boards changed every year or two, with succeeding state administrations, and there was no opportunity to develop anything like a continuous and consecutive policy with regard to admissions, or the conduct of licensing examinations. They were handicapped by the fact that no written examination can possibly determine whether an applicant is qualified to practice medicine. You know from your daily experiences in the ward and dispensary that the quality and ability to make a satisfactory examination of a patient and to weigh evidence and to arrive at a diagnosis are not things that can be determined merely by a written test. A man may memorize a textbook or even a quiz compend, and write the answers on paper, but when confronted with the problem of examining a patient, unless he has actually been experienced and skilled in doing those things, he cannot make the proper examination or take a proper history, and therefore he does not have a foundation on which to make the diagnosis.

To conduct the proper sort of practical examination is obviously a very tedious thing. It takes a great deal of time and effort, so that suitable patients are available for examination and to provide adequate supervision for the stu-

dents. Facilities of this sort have never been provided for the state medical boards. So far as I am aware, no state has ever appropriated from its own funds a single dollar to provide for the administration and enforcement of its medical practice law. The state says in substance: We want to protect our people from ignorance and incompetence masquerading as medical skill. We appoint a board of examiners to examine every applicant for a license. We forbid anyone to practice who is not licensed. We give this board no money. We are unwilling for such protection. Safeguarding our public is something we are not sufficiently interested in to justify the expenditure of a dollar of the peoples' money. If we can squeeze something out of these prospective doctors in the way of examination fees, they may be used by the board, but that is all. Of course, no public official expresses it in just those terms, but that is the substance and the effect of all the medical practice laws in existence in the United States today.

Still a third handicap was felt by these boards. Since they could not subject applicants to a practical examination, they really had to rely upon the kind of training and education that the candidate had had before he came up for examination. The examination became little more than a rubber stamp at the end of a medical course, but in order to determine whether the candidate had had a satisfactory education it became necessary to know something about the school from which he came. Obviously it was all-important to know which schools were giving satisfactory training and which were not. Again, however, these medical boards had no means for making such an inquiry. They had no funds to pay for the inspection of schools. Since candidates for licensure might come from all parts of the country, a nation-wide survey of the medical schools was clearly needed. Such a study would require funds and trained personnel, neither of which was at the disposal of the state boards.

Thus, at about the beginning of this century, we had 160 or 170 medical schools in the United States, some of them so meagerly equipped that they scarcely consisted of anything more than the equipment that I mentioned; that is to say, a hall with a stove and blackboard and a few chairs, the entire instruction being given by means of lectures without clinical experience whatsoever. The only laboratory which most of them had was the laboratory of anatomy, and that was not well used. Cadavers were not well cared for, and the students were compelled to spend a certain amount of time in making a dissection, and they usually got through it as quickly as they could without any very careful study or supervision.

Just at that time, most opportunely, the American Medical Association was reorganized, and instead of being merely a gathering of physicians which met once a year to discuss scientific papers, it became a federation based upon the representation of county and state units, and a permanent organization was set up, first of all, merely for the publication of *The Journal.*

Dr. George H. Simmons, who was the Secretary and the Editor of *The Journal,* realizing that the medical profession must assume responsibility for the training of physicians, began to study the situation to find out what was actually being accomplished in the preparation of medical students. The only information that was accessible was in the printed catalogs of the various medical schools, so he collected and analyzed them, seeking to discover, first, whether there were any educational requirements for admission to the medical school. For the most part there were none. Anybody could enter a medical school without having graduated from a high school, in some cases, without having attended a high school. He found out, also, that in their faculties there were none but practicing physicians. Medical sciences were advancing rapidly and a doctor whose practice was large and exacting could not be expected to come into the medical school for an hour or two twice a week and teach a course in laboratory chemistry. He did not have the time to prepare himself for it. He did not have time to prepare the laboratory or the materials or the apparatus that were needed, and yet that was the way chemistry was being taught, if it was taught at all.

Dr. Simmons felt it was necessary that there should be some continuing agency invested with the power to study the medical schools throughout the country, so that the medical profession and the public might know what sort of preparation a prospective physician might secure.

It was at his suggestion that the Council on Medical Education was formed in 1904, and Dr. Nathan P. Colwell, well known to most of you, was appointed as the Secretary. The first thing that he did was to visit every one of the 166 medical schools of the country. He described to the Council and to the American Medical Association the conditions which he found. The Association did not yet feel justified in making a public classification of medical schools. It

preferred to allow some time for needed improvements. Two years later the Council made another survey of the country on the basis of which all the medical schools were classified in three groups: A, B and C. The schools rated A were those which were regarded as reasonably satisfactory. The schools rated B were not satisfactory, but by making definite and substantial improvements, they might become acceptable.

The schools that were labeled Class C were utterly unsatisfactory and, in the judgment of the Council, there was no way in which they could be made acceptable except by a complete reorganization.

When these facts were published by the American Medical Association in 1907 there was manifested a great deal of resentment and hostility, first, on the part of the schools that were being criticized. They disliked being told they were not good schools, and they especially disliked to have the public told of their shortcomings. They attacked the medical profession vigorously, alleging that it was a medical trust, that it was trying to reduce the number of physicians in order to better its own graft, and that it was trying to make it impossible for a poor boy to get a medical education, and all that sort of thing which you may have read or can easily imagine.

If no one except the poor medical schools had objected to the classification by the Council it would have made little difference, but the trouble was that the public generally sympathized, as they very often do, with the underdog and, not knowing very much about it, the newspapers and editors joined in the clamor, attacking the American Medical Association as an arbitrary and despotic institution which was trying to drive the weaker schools out of business and prevent poor students from studying medicine, all in the interest of maintaining more power and more prestige in the hands of a small clique.

What would have happened if the American Medical Association had gone on alone, I do not know, but what did happen was this: The very wise Chairman of the Council on Medical Education felt it would be extremely helpful if the discoveries of the American Medical Association could be confirmed by some disinterested agency outside the medical profession which could not be accused of being partisan in this controversy, and whose findings and opinions would command the respect of everyone. He went to the President of the Carnegie Foundation for the Advancement of Teaching, which had just recently been organized, and had already made some studies in the field of college education, and asked Dr. Pritchett whether he would be willing to make a survey of the medical schools of the United States under the auspices of the Foundation. Dr. Pritchett consented, and for this purpose employed Dr. Abraham Flexner. Dr. Colwell, who had already covered the ground twice, accompanied Dr. Flexner on most of these visits, and aided him in his investigations.

In 1910 the Carnegie Foundation published its report on medical education, which depicted the situation so convincingly and so pungently that it was quoted in the newspapers from Maine to California. It carried weight with the public, because it came from a source which could not possibly be prejudiced in favor of the medical profession. Consequently, a tremendous popular sentiment was aroused in favor of better medical schools, better training for physicians, and higher standards of licensure.

In the few years following the publication of that report a very considerable number of states modified their law or rules so that no one could be admitted to the licensing examination except the graduate of a school rated Class A by this Council. That, of course, was a very great help, because if the man could not take the licensing examination in certain states his time in the medical school had been wasted. A good many states which did not enact a law restricting the license to graduates of Class A schools adopted rules and regulations of their own which had the same effect, so that in the four or five years following 1910 a great many of the states protected themselves against ignorance and incompetence by making it impossible for anyone except the graduate of a Class A school to take the licensing examination.

As a result, also, of the publications of the Council, reenforced by the publication of the Carnegie Foundation, there was a very great improvement in the medical schools. At the same time, there was a very great reduction in numbers. Those schools that had been rated Class C, for the most part, either merged with some other schools, or closed their doors. Some of them struggled along and raised themselves to the level where they could be rated as Class B. A few of them were able to exist by reason of the laxity of certain states.

Then came the war, during which it was obvious that we had no time to deal with the problems of medical education, important though they were. Afterwards, the educational institutions had been so upset and disturbed by the

conditions prevailing during the war that it seemed necessary to give them a certain amount of time to recuperate.

However, certain very great and substantial gains had already been made. In the first place, it had been recognized that a purely proprietary medical school, one controlled by a small group of doctors for their own benefit and their own interest, even though they did not profit greatly in a pecuniary way, was not in the public interest. Medical education, like other forms of education, should be brought under the control of those institutions which are organized for purposes of education in the public interest, rather than in any private interest. Most of the medical schools, not all, but very nearly all, by 1920 had made some sort of affiliation with a university. The degree of unification achieved by these affiliations varied very widely. Some were entirely satisfactory, others less so, but as a matter of public policy the principle was recognized that medical schools must be conducted as educational institutions in the interest of the public, and not as professional perquisites serving any private interest.

A second great advance lay in the recognition of the fact that some general education and scientific training were necessary before entering upon the study of medicine. Preliminary requirements were generally adopted by the schools and licensing boards, so that since 1918 all acceptable schools demand a minimum of two years of college, including the specified subjects, physics, chemistry, and zoology.

Another thing that had been gained was the recognition of the fact that the laboratory sciences, anatomy, chemistry, physiology, and the newly introduced sciences of bacteriology and pathology, must be taught by men who were devoting their lives to those special fields, who were teachers by choice, thoroughly trained and willing to devote themselves to the study and investigation of those sciences which they professed. So we had, in the preclinical medical sciences, entirely replaced the practitioner type of teacher with the man who had chosen teaching as his vocation and who had thoroughly prepared himself in his own field, whether it be anatomy, chemistry, physiology or pathology.

Fourthly, it was recognized that medicine could not be taught by lectures alone, that medicine in all of its clinical branches must be taught through intimate contacts with patients, that the student must be admitted to the ward and to the dispensary, and permitted to examine patients under supervision, participate in their treatment, and to learn what it is to actually take care of the sick.

While that was accepted in principle, the degree to which it could be carried out and made effective varied very much, and there were some institutions which were fortunate in having very close affiliations with hospitals where clinical teaching had always been stressed. There were many others where connections with hospitals were tenuous, meager, unsatisfactory, and where clinical teaching still remained more of appearance than of reality.

These conditions, together with the advancing standards in medical education, made it seem necessary to have a comprehensive review of the entire situation in order to find out just where we are and just where we are going. Four years ago, the Council on Medical Education and Hospitals of the American Medical Association undertook this study. They began by sending to every one of the medical schools a set of papers, which unfortunately had to be called questionnaires, but the real meaning of those papers was that they were reports from the officers of the school and from the members of the faculty on the character of the work which was going on in the school, and more particularly from each member of the faculty of professional rank a report on his own personal history, training, and qualifications.

After the receipt of this information from the school, which was in the nature of a report signed by the officers of the school itself, we employed Dr. Herman G. Weiskotten, of Syracuse, to visit all of the schools in the United States and Canada and make a personal investigation to supplement the reports. It was necessary in many cases to check up these reports and find out whether they had been accurately answered. It is surprising how easy it is for people to misunderstand questions, even though one tries very hard indeed to make them simple and intelligible.

The observations of Dr. Weiskotten, together with our reports and the published records of the institutions, gave us an unusually complete picture of the activities of each of the medical schools. Certainly, it was the most thorough investigation of this sort that had ever been made. In each one of the medical schools visited our inspectors spent at least three days in interviewing the various teachers, examining the work in the various laboratories and hospitals,

and also studying the whole problem of organization and administration with the officers, such as the dean and the president of the university.

On the basis of those findings, the Council then issued to each one of the schools a report on its activities, which was not based upon an ideal or arbitrary standard set up by the Council, but simply a comparison with the activities of other schools. We included in this report, because we had information on those particular points, some ninety-six items, but on each one of these items all of the schools were arranged in a rank order. For example, it was the size of the budget or the number of the books in the library. Take the case of the books in the library: all of the schools were arranged in order according to the number of volumes in their libraries. Then the number of schools was divided into ten equal parts, so that each school was represented as being in the first, second, third or fourth decile, as the case might be. The schools were not told how many books they should have in their library, but they were told whether there were ten schools that had larger libraries than they had, or fifty or sixty schools that had smaller libraries.

The same plan was followed with all the other items included in the report such as organization and administration; the financial set-up; the budgets; the salary list; space and equipment of the various laboratory departments and clinical departments; the training and experience of the members of the faculty; the extent to which they were engaged in investigation, their activities as members of scientific societies, or contributors to scientific journals. All of these different subjects were discussed and presented in the form of a graph or pattern map.

That represents really the conclusion of at least the description of the Council's activities up-to-date, but I want to return just for a moment to the question I asked you at the outset, and that is again asked, why should the Council on Medical Education, which is a branch of the American Medical Association, be engaged in this work of appraisal? We have no legal power. We have no legal status. We have no authority. Nobody asked us to do this job. We simply went out to do it because there was nobody else doing it and, in the judgment of the American Medical Association, there was no one else who could do it. The state boards, upon which the responsibility rested logically, were unable to conduct any such survey or establish any such method of appraisal of medical schools, and in order to help them to fulfill their function of protecting the people from ignorance and incompetence, the medical association, which represents the medical profession of this country, has voluntarily paid for the maintenance of the activities conducted by the Council on Medical Education and Hospitals, the chief of which is this appraisal of medical schools.

CHRISTIAN FENGER*

By ALTON OCHSNER, M.D.
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Christian Fenger, the father of pathology in the Middle West, was born in Copenhagen, Denmark, on November 3, 1840, the son of Kammerraad Hans Fritz Fenger. A love of the natural sciences prompted him to study at the Polytechnic Institute with the idea of becoming a civil engineer, but after a year of study he yielded to his father's wishes and began the study of medicine. Apparently he was a good student in school, because he received very high marks. He earned part of his way through school by teaching in high school and later by giving instructions to medical students in anatomy and by coaching dentists for their examinations. This was necessary, because he was one of twelve children, of whom seven were sons. While he was still a medical student, war broke out between Denmark and Germany, and in the year 1864 he served as assistant physician for a battery at Assens. Following the close of the war he continued the study of medicine and passed the examination for the practice of medicine in 1867 with honor. For two years after his graduation he served as amanuensis to Dr. Wilhelm Meyer in his clinic at Copenhagen. His friendship with Meyer began during an illness which Fenger had had as a student. He collaborated in Meyer's celebrated investigations on adenoid vegetations of the nasopharynx. In 1869, he became an intern at the Royal Friedrik Hospital in Copenhagen, where he stayed for two years. Professor Saxtrop, who was chief of the surgical division, had opposed his appoint-

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ment because he had been assistant to the "German Meyer." For the two years that he served as an intern in the hospital he said that not a word was spoken between Professor Saxtrop and himself. During his internship he wrote an essay on subperiosteal operations, and also performed experiments on gunshot wounds of horses at the Royal Veterinary College and constructed instruments for the localization and extraction of bullets from the tissues. A paper based on these experiments, entitled "Concerning the Endoscopy of Gunshot Wounds," was responsible for a grant from the Royal Danish Minister of War, which assisted him in taking part in the Franco-Prussian War of 1871. In January, 1871, he was appointed as surgeon in the Red Cross Ambulance Corps and served in that capacity throughout the war. It was during this time that he wrote a report on the endoscopy of gunshot wounds. After the war he went to Vienna, where he studied pathologic anatomy and surgery under Professor Billroth for a short time. Following this he returned to Copenhagen, where he became prosector to the Copenhagen City Hospital, which position he held four years. While there he wrote his thesis, "On Cancer of the Stomach with Special Reference to Its Structure, Development and Extension," for the degree of Doctor of Medicine. This contribution, which is still a masterpiece, is based largely on postmortem investigations and is particularly valuable because of the accurate description of the modes of extension of the lesion and involvement of the gastric nerves. A number of other papers on hydronephrosis, gonorrheal rheumatism, endoscopy of the urethra, and stenosis of the pulmonary orifice were also written, for which he received the Smith Grant for Advanced Study. In 1875, because of the illness of Professor Rasmussen, he was appointed Docent in Pathologic Anatomy. He was told by Professor Reiz, who held the examination for the students whom Fenger had instructed, that Fenger's students passed as good examinations as those who had done the work under his own (Reiz's) direction. Shortly after this, Professor Rasmussen, who was head of the Department of Pathologic Anatomy, died, and Fenger hoped to be appointed to the position. As, however, the place was given to Professor Karl Lange without competition, Fenger stated that he felt his road to an academic career was blocked. He, therefore, decided to leave Denmark for an independent position. In order to do so he had to borrow money from the mayor of the city, which loan he returned fourteen years later. His disappointment must have been great, although he says:

"I was not disappointed or depressed because I did not obtain the professorship in pathologic anatomy for the following reasons: I had always been greatly interested in surgery and had regarded the study of pathologic anatomy as a means of entering surgery as my final object, my work in surgery having already been commenced in the two years in which I had taken part. Assistant surgeon at the Friedrik Hospital I could not become because of my relations with Professor Saxtrop. The same position at the Community Hospital had been filled just as I had ceased to be prosector for that hospital. I consequently could not see any immediate opportunity to commence the further study of surgery. Inasmuch as surgery interested me more than pathology, it was in reality a help for me that Professor Karl Lange was appointed, because it freed me from the obligation of continuing pathology as my life work and gave me an opportunity to seek elsewhere the opportunity where I might be able to dedicate myself to surgery."

As he apparently felt that progress would be slow in Denmark and because his brother was a practicing physician in Alexandria, Egypt, in 1875 he went to Alexandria to take over his brother's practice while the latter went to Denmark to be married. After his brother returned to Egypt, Fenger became a member of the board of health, which was the sanitary council, and received the appointment as surgeon to the Khalifa of the District of Cairo, which was a salaried position under Dr. Beye, who was chief of medical affairs in Cairo. Here he investigated trachoma in the school children of the public schools. In 1876, he had dysentery and infection of the liver which compelled him to leave Egypt and return to Europe to recuperate. He was granted leave of absence with full pay during this time. As, however, the liver disease again appeared shortly after he returned to Egypt, he felt that he was compelled to go to a temperate climate. While in Cairo he had been physician for part of the American colony, among whom were certain American officers who had been brought in to help in the organization of the Egyptian army. Acting upon the advice of General Stone's wife, who was a relative of the poet, Longfellow, he decided to go to America, and also because an American officer, Major Irgens, who was on leave of absence because of illness, wished him to accompany him on sick leave, he came to the United States in 1877. He practiced ophthalmology for a few weeks in New York, during which time he operated upon several patients with cataracts. In commenting on these cases he stated, "Confound it, they all went blind." Possibly because of this and also because he received no inducement to

practice in New York, he went to Chicago with the idea of possibly continuing on to San Francisco, where he thought that he might practice ophthalmology. He told his nephew-in-law, Dr. Coleman Buford, that if he failed in San Francisco he intended continuing on to Australia, because "then he could go no farther west." Upon arriving at Chicago he was taken sick and was treated by a fellow countryman, Dr. S. G. Jacobsen, who advised him to remain in that city. Probably another important factor in his remaining was that his funds were practically exhausted. He lived in the Scandinavian part of the city and had very little practice. In the spring of 1878, he secured by means of borrowed money a place as physician at Cook County Hospital and began to give lectures and demonstrations in pathologic anatomy, "a science which was unknown to the physicians there." For the following year he served on surgical services when his surgical colleagues were on their vacations. He later was appointed as surgeon to Cook County Hospital and while in that capacity introduced antiseptic surgery as practiced by Lister. In 1880, he became curator of the Rush Medical College Museum. In 1884, he became Professor of Surgery in the College of Physicians and Surgeons and Surgeon-in-Chief at the Passavant Hospital and German Hospital, when these two hospitals were founded. In 1893, he became Professor of Surgery in the Chicago Medical College, which later became Northwestern University Medical School. In 1899, he became Professor of Surgery at Rush Medical College. In 1878, he married Caroline Abiltgaard, of Clifton, Illinois, who was also a native Dane. To this union were born two children, a son, Frederick A. Fenger, and a daughter, Augusta Maria Fenger. In 1891, he received the order of the Knight of Dannebrog from his Royal Highness, King Christian IX, of Denmark.

Fenger was a prodigious worker. In all, he published approximately eighty original articles, of which seventeen concerned the genito-urinary tract, twelve were gynecological, seven orthopedic, six thoracic, and three cranial. His doctor's thesis on carcinoma of the stomach is still a masterpiece. It is one hundred and twenty pages long and is beautifully illustrated. Nicholas Senn, at a testimonial given to him by approximately five hundred of his medical colleagues on the sixtieth anniversary of his birth, on November 3, 1900, said of Fenger's thesis:

"He showed by his careful investigations that a direct relationship exists between the location of the disease and branch of the pneumogastric nerve. In other words, in explaining one of the clinical phenomena, pain, he demonstrated the involvement of the nerves by the carcinomatous process when the disease is at all productive of pain. * * * He is so familiar with the functions of every organ in health that any disturbances caused by disease are quickly recognized, a knowledge upon which depends his acumen as a diagnostician. Take him into a chemical laboratory and he will make analyses and experiments that would fascinate the students and astonish the director. The microscope is our guest's most constant and nearest companion. There is no operation he has not performed, no region he has not invaded. Twenty years ago he taught us how to explore the brain systematically and safely in search of abscess. To him belongs the credit for having led the way in this country to successful surgery of the lung. His articles on surgical affections of the biliary tract have become common property to be read in all living languages. He stands next to Simon and James Israel in renal surgery. There is no one who would pretend to know half as much as he does of the surgery of the ureter. If our guest has any specialty in surgery, it is the abdomen and pelvis. He has performed more difficult pelvic operations than any other teacher of gynecology in this city. He was the first man in Chicago to perform vaginal hysterectomy for carcinoma of the uterus."

In 1881, he read an article on the drainage of lung abscesses. In 1887, in the *Journal of the American Medical Association,* he published an article on antisepsis in abdominal operations. In this study careful bacteriologic examinations were made of material used in operations. In preparation for operations each participant took a sublimate bath, 1:2,000, and put on sterilized cotton suits. The hands and arms were scrubbed for five minutes with a brush, warm water, and green soap, and then washed for a half minute in 1:1,000 sublimate solution. The operative area received practically the same treatment. Everything coming in contact with the patient was cultured, and he demonstrated that the skin, sponges and other substances used were sterile. In 1883, he published a rather extensive article on appendicitis in which he advocated drainage in almost all cases. He did extensive experimental work on ureteral surgery, on floating stones in the common duct, and advocated choledochotomy in such cases.

He was a man who had the courage of his convictions, as illustrated by the paper which he presented before the Chicago Medical Society and which was published in the Chicago *Medical Recorder* in 1898, entitled "Remarks on Surgery of the Bile Ducts." Apparently some of the statements which he had made in a previous presentation had been doubted by Dr. Beven. In his discussion he says:

"I have no time for and dislike controversy. Before reading his paper, Dr. Beven made it known to me his

intention of questioning the anatomic relation of the common duct and portal vein as set forth in my paper on the treatment of gallstones. I endeavored to demonstrate to him that he was in error. As he still holds to his opinion, I feel it is encumbent upon myself to set him in the matter aright. It is a serious accusation to state that I am mistaken in anatomy by claiming that the portal vein comes up on the anterior surface of the common duct, especially so as I had brought out some points of the pathologic surgical anatomy of this region never before described, and I cannot allow suspicion of unreliability to rest upon any of my writing. In my paper I have illustrated and described the pathologic surgical anatomy of the field in operating upon the common duct."

Apparently the controversy resulted because of the difference in conception, as Beven's descriptions were made considering the individual in the erect position, whereas Fenger's descriptions considered the patient in the horizontal position as seen on the operating table. To quote him further:

"Dr. Beven has evidently read my article carelessly if he doubts my statement that the portal vein in its terminal course is found located on the anterior (or inferior) surface of the right hepatic portion of the common duct. * * *

"Dr. Beven presents a specimen of liver and bile ducts with the latter together with the vessels dissected out and the vein emptied. When the ducts and vessels are loosened from their surrounding, it is practically impossible to judge of their relative positions, because they are then easily displaced. * * *

"Dr. Beven has made some forty dissections and presents as a result a series of drawings of the bile ducts and their surroundings. These drawings do not differ materially from the time-honored classic illustration of the territory to be found in the anatomic atlas. They differ only in that they are less correct than the classic ones, inasmuch as they are entirely schematic and do not give any dimensions. * * *

"The beginner in the surgery of the bile ducts who in a given case of stones in the gallbladder or ducts would rely upon Dr. Beven's anatomic plates as guides in his operation would be much deceived and very much at sea. He would find his descriptions of the case so entirely different from the normal anatomic conception that he would be at an utter loss to find his bearings. * * *

"In conclusion a word relating to the phrasing of Dr. Beven's criticism of my paper, he 'feels sorry' for me that he must 'do his duty by the profession' by 'correcting my erroneous anatomy' because my paper has been widely read and attracted attention. This with my previous reputation for reliability might mislead those who read my paper, etc. I need not suggest that such language is not used in the best scientific medical literature. Time and experience might prove the tenor of the doctor's future record."

Preparations for his diagnostic clinics were painstaking and labored, frequently lasting into the small hours of the morning, and in presenting a subject he presented everything known on a particular subject from the very beginning. His operative work was done well, but he did not operate rapidly. He interpreted pathology as he proceeded. His days were filled completely with activities. To quote his nephew, Buford:

"There was no day which was not completely filled and during the busy periods it was not uncommon for Fenger to start operating at one hospital at 8:00 o'clock in the morning, at another at 10:30, and still another at 1:00 o'clock, perhaps reaching the office at 3:00 p. m., have a light lunch, see all the patients he could, dismiss quite a number of them, asking them only to come some other day or in the evening, go with one or two physicians in consultation, get supper at 9:00 or 10:00 o'clock, and go soon to his library where, in the thick of smoke and with a pitcher of lemonade in front of him, he read until very late. When his younger assistants found difficulty in keeping up with him, he reminded them that from the time he entered the gymnasium for about thirty years thereafter he seldom took off his clothes to go to bed."

He spoke eleven languages, swore volubly in most of them, subscribed to journals in many tongues, specializing in bacteriology, pathology, genito-urinary, nervous and mental diseases, internal medicine, as well as surgery. He was a careful critical reader and always made extensive notes of his readings, which were classified and used whenever needed. He was not a fluent speaker, and although at first it was difficult to follow him because of his hesitating speech, his clinics and rounds were always well attended. Dr. Fenger was very modest and abhorred publicity of any kind. When informed that he was to be honored by a testimonial banquet on his sixtieth birthday, he blurted out, "Hell, I'm not dead yet." It is stated that while testifying as an expert witness and being cross-examined by the opposing attorney, the following conversation took place:

"Doctor, how many postmortems have you performed?"

Fenger bruskly replied, "I don't know."

"Well, have you performed one?"

"Yes."

"Two?"

"Yes."

"Five?"

"Yes."

"Have you performed ten?"

"Yes, ten thousand."

Fenger knew nothing but work. To quote Senn:

"Fenger was a tireless worker. He seldom allowed himself a vacation. He found the greatest happiness

in the operating room, the morgue, the laboratory, and the library. He was the first teacher of modern pathology in the city (Chicago). He was an expert in the use of the microscope as an instrument of scientific investigation and an aid to diagnosis. All diseased tissue he removed was subjected to scrutinizing microscopic examination, and in all obscure cases he resorted to the use of this instrument before he made his final diagnosis. He was also an artist. Any operation of any magnitude which he performed he illustrated by colored blackboard drawings portraying accurately the pathologic condition, surgical anatomy, and technic of the operation. As a surgeon Fenger was conscientious, painstaking, and thorough. He did not operate for the sake of operating. He looked carefully for contra as for indications for an operation. He detested all attempts at display of manual dexterity. He operated slowly, but deliberately. Every one of his operations was a careful anatomic dissection. He has performed more difficult operations than any other surgeon in this country. Fenger was a striking personality, and in a throng of people his presence could not fail to attract attention. He was of medium height with a physical constitution that did credit to his ancestors and the country of his birth. He was a blond, a perfect type of the hardy Norseman. His commanding forehead and ruddy face were deeply furrowed, not by the ravages of time, but carved from the effect of unceasing mental toil. His face reflected the image of a deep thinker and right scholar. His azure blue eyes could smile like the spring sun when he was in good humor, but when his passions and feelings were wrongly aroused, they became dark so as to bring into submission his most formidable enemies."

Dr. Fenger enjoyed the reputation of being one of the eminent consultants of his day. Dr. Franklin Martin, in "His Joy of Living" says that in one of his cases

"It was decided that I should call Christian Fenger, then the outstanding surgeon in Chicago. Fenger came over from the North Side in his shabby little buggy, drawn by the old horse that possessed enough horse sense to read his august driver's mind when he drove with one rein or none. The distinguished scientist was genuinely interested in his young confreres and their predicaments. Grunting and expressing his thoughts in several languages, he finally blurted out that the temperature must be the result of the improper evacuation of the anchored tumor. He advised the use of a Schultz curette, a spoon-like instrument to scrape off the lining of the tumor and remove any pyogenic material. Bishop produced the instrument from his German kit and Professor Fenger, the dear fellow, stayed with us, as always oblivious to the loss of his valuable time, and watched the curettement. Each time he brought out from the depths of the tumor a spoonful of pyogenic material, he enthusiastically expressed his approval. During the manipulation a little abscess was seen in the abdominal wall near the seat of the operation, opened and emitted a teaspoonful or more of pus. This interested our consultant very much. The long process was terminated and the admiration of our local group for the distinguished Dane was sealed as never before."

Fenger always feared pneumonia. During the winter he wore two suits of heavy underwear and after operations changed to dry underwear. Because of his fear of pneumonia, it is significant that he died after a week's illness of that disease on March 7, 1902.

With Fenger's death the world, but especially America, lost one of its greatest scientists, one who was, as described by Le Count, "the incarnation of the scientific spirit in surgery." Although he has ceased to live, his influence on scientific medicine is still and always will be felt.

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ANATOMICAL AND FUNCTIONAL RESULTS IN FRACTURES OF THE PELVIS*

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The primary purpose of this paper is to bring to attention the consideration of fractures of the pelvis from an anatomical and functional standpoint. It naturally is necessary to consider the pelvis as a whole in the discussion of fractures in this region. However, in this discussion, your essayist wishes to bring to your attention only the commonest fractures of the pelvis, namely: fractures of the rami of the ischium on one or both sides associated with or without fractures or dislocations through the sacro-iliac joint, on the same or opposite side, and further to emphasize the contrasting male and female pelvis from the anatomical and functional results that should be expected in each.

The force which causes pelvic fractures may be direct or indirect; it is most frequently a crushing force. The fracture may be of almost any variety. Fracture through the acetabulum and through the ascending rami of the pubis is the commonest type[1] [2] Occasionally fractures

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of the anterior-superior spine and fractures through the wing of the ilium occur. Fractures of the acetabulum associated with or without dislocations of the head of the femur are likewise not uncommon. These latter types are mentioned, not for the purpose of detailing treatment, but only as a fracture problem of the pelvis as a whole.

The most serious complications in connection with fractures of the pelvis are injuries to the abdominal viscera, such as rupture of the bladder, particularly when full, by sharp spicules from one or more of the fragments.[1 2 3] If this complication occurs, it is easily recognized by blood in the urine or feces or both. It is usually associated with extreme shock on the part of the patient and the gravity of this injury is so great that the fracture becomes a secondary consideration in the treatment.

Fortunately, in the majority of pelvic fractures the displacement of the fragments is not severe enough to cause visceral injury.[4 5]

The clinical basis for the presentation of this paper is a series of twenty-six cases treated in private practice. Ten of the cases involved the female pelvis and all were produced by automobile accidents. Of sixteen male pelvic fractures in the series, twelve were produced by automobile and four by industrial injuries. The type of fracture varied little, if at all, in industrial injuries.

Since I do not practice in an industrial area, the number of industrial fractures of the pelvis is naturally small. However, we are blessed with good roads and many automobiles, and automobile injuries in this series are high. Injuries from this cause in men and women patients are about equal and of the same type.

The first essential consideration, of course, is to make as accurate a diagnosis as possible, by physical examination aided by careful stereoscopic x-ray study of the pelvis. A careful general physical examination should always be made after an accident, and the question of the presence or absence of a pelvic fracture or its visceral or other serious complications should be ruled out. In this series of twenty-six cases, six were accompanied by rupture of the bladder. One of the six proved fatal, in spite of all routine surgical care. The other five healed and eventually recovered. This series dates from April, 1934, up to the present time.

Early in the spring of 1935, your essayist was confronted with three patients of this series, women about the ages of 25 to 30 years, an age period very important to the female pelvis in this stage of life, because of the function of childbirth.

Whether or not the importance of this function had been profoundly impressed upon the writer prior to this time cannot be definitely stated. However, the anatomical and functional results expected to be performed by the pelvis at this particular time was most forcibly brought to his attention, in treating the above cases.

A young woman 25 years of age, mother at that time of two children, received a severe crushing fracture to the pelvis involving both the superior and inferior ramus, which produced a severe deformity of the pelvis, as will be shown by the lantern slides. An extremely distorted outlet of the pelvis was produced, which, if left as it were, regardless of the fact that it probably would have healed, would have made normal childbirth impossible.

We undertook to set this fracture in the manner which had been used in earlier cases. She was placed upon a Bradford frame, suspended in the canvas hammock with traction on both legs. Careful x-ray check-ups failed to show a satisfactory reduction until the method of treatment advocated by Dr. S. A. Jahass,[4] of New York City, who utilized the lever principle, was employed. The lever principle of reduction is brought about by applying a cast to both lower extremities in which is incorporated three turnbuckles.

The details of application have already been described and the technic will not be gone into again at this time as no doubt all of you are familiar with it.

By this technic, it was possible to restore the outlet of the fractured pelvis to normal. The same technic has likewise served in a total of twelve cases most satisfactorily.

In consideration of the importance of anatomical and functional results in fractures of the pelvis in which the outlet has been distorted, a method of reduction which will assure us of anatomical restoration should be our goal.

The method of choice should be that outlined by Dr. Jahass or others,[5 6] or the Jones traction splint.[7] Particularly are these splints and the Rogers Anderson well leg splint very useful in treatment of fractures of the acetabulum, with impacted or dislocated heads of the femurs.

The type of treatment can be decided upon only after a thorough study of carefully made stereoscopic x-rays, and the method decided upon should be one which will best restore and preserve the continuity of the pelvis with particular reference to the anatomical restoration of the pelvic ring. Such a restoration will obviate sequelae which may appear a year or more later, involving particularly the posterior region

of the pelvis and the sacro-iliac and the lumbo-sacral joints.

In treatment of fractures of the pelvis, nearly perfect anatomical and functional results should be obtained in order to prevent posterior injuries. The restoration of the normal outlet of the pelvis is more important than has heretofore been stressed in the literature.

The methods of reduction which are now at our command can restore the fractured pelvis as nearly to its position before the fracture as one could possibly expect.

It is a well known fact that posterior injuries are a great deal more disabling than are anterior, particularly those involving the pelvic ring. However, in fractures in which both the posterior and anterior structures are distorted, the goal of our treatment naturally should be a restoration to normal.

Too little emphasis has been stressed in prior writings on this phase of the question in discussion. We have been satisfied with results, particularly in fractures of the male pelvis, in which a great deal of residual deformity has remained, but the individual has been able to carry on his occupation in spite of this condition. The majority of fractures of the pelvis heretofore have occurred in the male, but with the advent of the automobile and the type of injuries it produces, fractures of the female pelvis has become common, and this has brought to our attention the importance of restoring the outlet to normal. This can, in the majority of cases, be accomplished.

SUMMARY

(1) Restoration of anatomical and functional results in fractures of the pelvis should be our goal and aim.

(2) This can be accomplished by careful examination and proper selection of a method of treatment suitable to the fracture involved. The method and technic of Dr. J. A. Jahass are suitable in the majority of cases.

(3) Let me re-emphasize the fact that the prime consideration in treatment of the fractures of the female pelvis is the restoration of the normal dimensions of the birth canal.

(4) These opinions are based on a study of twenty-six selected cases.

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DISCUSSION (*Abstract*)

Dr. W. K. West, Oklahoma City, Okla.—I have not used the method described by Dr. Carruthers. It is very plain, from the slides, that his results have been most satisfactory. The majority of the cases shown were fractures through the rami, either unilateral or bilateral.

I wish to stress the treatment of another type of fracture which he did not emphasize, namely, fracture through the acetabulum with the head of the femur carried part way through the fracture crevice. With this type, if seen early, excellent reduction can be expected from a Kirschner wire traction in two planes: (1) longitudinal traction with wire through the lower condyle of the femur; (2) lateral traction with the wire introduced through the trochanter.

The success of this method depends largely on the time that has elapsed since the injury. If seen within the first few hours, very satisfactory anatomical reduction can be expected.

Dr. Earl D. McBride, Oklahoma City, Okla.—I wish to direct attention to a simplified method of well-leg traction which I have used for a number of years with a great deal of satisfaction, a method which does not require any complicated or expensive apparatus.

In this method a full leg plaster spica is applied to the well leg. On the leg to which traction is required, a Kirschner wire can be inserted through the lower end of the femur so that an extreme amount of weight may be applied with an overhead frame and pulleys, leaving the counter traction to the pressure on the rigid plaster spica of the well side. In the Malgaine's type of fracture of the pelvis in adults I have applied as much as fifty pounds of traction weight to bring the pelvis into normal alignment. In children I have inserted the bars of a Thomas splint and used adhesive for fixed traction. This affords the great convenience of being able to transport the child from the bed.

I have had better success in reducing fractures of great displacement of the ilium by this method than by any method that I have tried.

Dr. J. Albert Key, St. Louis, Mo.—I object seriously to the principle that an attempt should be made to obtain anatomical reduction in fractures of the pelvis. It is true that there are occasional instances where reduction is desirable and here the double cast with the multiple turnbuckles or the well-leg traction splint is useful. However, such cases are rare and the application of either the double cast or the well-leg traction splint should not be used routinely, but should be reserved for these few cases. Otherwise, one is apt to cause complications due to pressure on the inner aspect of the upper thigh or to infection from the introduction of skeletal traction.

BACKSIGHTS ON AMERICAN PUBLIC HEALTH*

By T. H. D. GRIFFITTS, M.D.
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As an engineer takes backsights as a necessary reading in determining the elevation of the new station, so, in determining our elevation in public health, backsights are necessary, using an assumed datum as the bench mark.

Apparently, except for disease which they brought with them, early explorers, adventurers, home and fortune seekers, rightfully feared most the weather hazards, deprivation and scalping. Much speculation has been indulged in as to whether the primitive American suffered from pestilential diseases by which the white colonists were attacked. Until the development of relatively large groups of populations which later became cities, such as Philadelphia, Boston, New York and Baltimore, records of sickness and deaths were not preserved, nor were there regularly constituted health authorities.

As "necessity is the mother of invention," so it may be said that "calamity is the father of reform." As is well known, the city of Philadelphia, with a population then of 30,000, suffered the loss of 4,002 souls from yellow fever in 1793 (August-November, inclusive). This, quite naturally, brought much animated discussion of the probable origin of the disease. The medical profession was divided on the subject, but there was almost immediately adopted a law providing for a board of health. Two of the five members were to be physicians and all were to be appointed annually by the Governor. Under the provisions of the first health law adopted, and amendments there to in 1806,† the board of health was required

"to meet once every day between the first of June and first of October, and also when specially convened by the President, or by any two of the members; and is vested with full power to make general rules, orders, and regulations, for the government of the lazaretto, and the vessels, cargoes, and persons there detained, or under quarantine; and of the health office and public hospitals and to appoint * * * a health officer."

Vessels coming from ports at which a malignant disease prevailed were detained

"so long as the board of health shall deem necessary, but not exceeding twenty days, * * * but if disease has occurred during the voyage, or while in quarantine, the vessel is to be detained such further time as the board may deem necessary, the cargo to be unladen and purified; and the crew, passengers, cargo and luggage (except such cargo as rum, wine, salt, sugar, spices, molasses, mahogany, manufactured tobacco, etc, which could be taken off in lighters) shall not be suffered to enter the city before the first of October, without license from the board."

Refusal to answer the questions of the physician, or deception, drew a "penalty of $500 and imprisonment at hard labor of not less than one year and not exceeding five." This law, enacted at the first session of the Legislature after the "awful, mortal epidemic of 1793," was almost entirely predicated upon the supposition of the

"importation of the fever of 1793, and of epidemics generally; and hence while numerous provisions were made for preventing the introduction of malignant diseases from abroad, little or no attention was paid to guard against their origin at home."

To quote further from the same source:

"The repeated occurrence of the epidemic naturally continued the discussion of the question of origin. The propriety of attention to the sources of production at home was made manifest, and a commendable degree of cleanliness in the city, in which it was before very deficient, has followed."

During the century following the inception of the idea that such epidemic diseases as yellow fever were introduced by ships, our national quarantine became well established through careful observations by a long list of science-devoted heroes. Time will not permit a roll call of these contributors from the old sailing vessel to the "China Clipper." Transportation becomes more and more important as a factor in the introduction and spread of disease.

It is obvious, then, that the continued discussions among leaders in Philadelphia after the yellow fever plague of 1793 resulted in two steps significant in American public health: (1) the supposition that yellow fever had been imported by sailing vessels and the necessity for quarantine regulations; (2) once introduced, the community had grave responsibilities in limiting its spread. Hence, it may be said that the "City of Brotherly Love" gave to us the ideas of our national quarantine and our local board of health.

Nor is this all that grew out of the yellow fever epidemics of 1793 and the following years. A common water supply for that city was first urged by Benjamin Franklin, and in his will it was directed that when the interest, arising from a legacy for a certain purpose, amounted to a certain sum, it should then be applied toward the provision of a public water supply. In 1797 petitions were circulated calling for action upon

*Chairman's Address, Section on Public Health, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

†Picture of Philadelphia, 1811.

the subject of a public water supply. There was a

"growing conviction in the public mind of the connection between the cleanliness of a city and its health; of the utility of a copious supply of water in case of fire, and for culinary purposes."

Several plans were proposed, but that offered by a Mr. Latrobe, an engineer, was accepted, and Mr. N. J. Roosevelt, of Soho, New Jersey, was given the contract to provide

"two steam engines, of a power to raise and deliver, at the height of 50 feet each, three million gallons of water in every twenty-four hours throughout the year."

The proponents met with much opposition from a "corporation" claiming infringement of their rights to "water the city," and from citizens who seriously doubted the possibility of utilizing steam in pumping the water.

"On the second of May, 1799, the first sod was dug, and although a dreadful epidemic fever prevailed in the succeeding autumn, the work went on without interruption, and on the 21st of January, 1801, the first water was thrown into the city."

Again quoting from "Picture of Philadelphia, 1811:"

"It may be mentioned as a striking fact that the malignant fever in 1801 and since that year has been chiefly, if not entirely, confined to those parts of the city and liberties, into which the water had not yet been introduced."

This was an interesting observation, and probably correct, as it would be expected that much storage of water in containers in and about homes and business places would have been discontinued, thereby eliminating many breeding places of *Aedes aegypti.*

So, out of Philadelphia's suffering came one of the greatest blessings of our American civilization, public water supplies. In this connection it will be recalled that about 100 years later another American city, New Orleans, abandoned her above-the-ground cisterns and secured an excellent public water supply. Of course, the character of the common water supply, *per se,* was not a cause of yellow fever in either case, but a public distributing system abolished the necessity for household storage of water and thereby eliminated many and prolific sources of *Aedes aegypti.* Yellow fever had its part in creating the demand for New Orleans' public water supply. It so happened that the latest epidemic of yellow fever in this country occurred mainly in New Orleans (1905), while cisterns were still in vogue.

While dwelling upon the relationship of diseases and lack of public water supplies mention should be made of cholera. This disease first appeared in this country (via New York) in 1832, and other epidemics occurred in 1835, 1836, 1858 and 1849, the latter epidemic being spread up the Mississippi Valley and reaching the Pacific in 1849 by means of the "gold rush." Introduction through immigrants and limited prevalence recurred in 1854, 1866, 1867 and 1873. Since the latter year only a few times have cases been imported, and no epidemics have occurred. As this disease is spread like typhoid, a potable water supply is the main prophylaxis against epidemics. Few physicians in this country today ever saw a case of cholera; none should ever see another case.

The medical student of thirty to forty years ago saw in some parts of the United States more cases of typhoid fever than of any other single disease. Will those of us who fought the "battle of flies" at Chickamauga in 1898 and saw the men swim in the creek from which drinking water was obtained ever forget the scene? It is not too much to expect that this disease will finally be a matter of history.

Smallpox, of all diseases, should be completely eradicated, yet there is only one enlightened country in the world having a higher number of cases annually than our own. This is an indictment against the intelligence of the public; yet, strange to say, the greatest prevalence now reported in the United States is from some of the Western states where "illiteracy" has a low rating. A good test of "literacy," or intelligence, at least, should be the exhibition of a vaccination scar. As evidence of slow progress, allow a quotation from a vital statistics report of one of the larger cities 128 years ago:

"Vaccination is rapidly dispelling the loathsome smallpox from the city."

A society was organized in that city in 1809 "for the promotion of vaccination among the poor." Is it believable that I recently saw a woman who acknowledged that she was 48 years old, had taught in the public schools of a metropolis for ten years, and had never been vaccinated, either successfully or unsuccessfully? It is probably true that our present laxity is due to the mild strain that has prevailed over a period of several years.

Of the chronic and deadly preventable diseases, the most satisfactory decline in rate is taking place with tuberculosis. Syphilis constitutes another story. There is no simple, effective method of control; it calls for the application of the greatest of public health statesmanship. Recorded history informs us that the

voyages of Columbus are credited not only with the discovery of America, but that they and succeeding ones carried to Europe incalculably more *Treponema pallidum* than gold. Whether or not the original bed of syphilis was America, as claimed, the disease was not recognized as an entity until the beginning of the great European epidemic in 1493. In this country the ravages of the disease were strongly brought to our attention and major steps were taken for lessening its prevalence during and following the World War. Moral suasion and educational efforts have failed to secure satisfactory results; medical inspection and personal prophylaxis are not the answer; padlocking public prostitution places and tolerating hetaerism fail. The plan promulgated by Parran in recent years has greatly stimulated renewed activity in the importance of this public health problem and offers a sound program of attack.

Of acute diseases, diphtheria has been largely robbed of its horror and responsibility for death by the general use of specific prophylaxis and therapy, as well as the employment of the Schick test; scarlet fever by the application of the Dick test for susceptibility, and the use of serum in toxic cases and improved drug therapy. Diarrhea and enteritis in children are greatly reduced. Other diseases, such as measles, whooping cough, and poliomyelitis continue to hold their secrets, more or less.

Our first national law relating specifically to public health protection applied to the chosen representatives of the people and the states:

"Sec. 34. Whenever Congress is about to convene, and from the prevalence of contagious sickness, or the existence of other circumstances, it would, in the opinion of the President, be hazardous to the lives or health of the Members to meet at the seat of government, the President is authorized, by proclamation, to convene Congress at such other place as he may judge proper." (R. S.; Act April 3, 1794, ch. 17, 1 Stat. L. 353.)

Similar procedure was provided in another act five years later (R. S.; Act February 25, 1799). This provided for the removal of revenue collecting agents to safe ports, the removal from the seat of government

"of any or all public offices to such other place or places as he [the President] shall deem most safe and convenient for conducting the public business."

The Chief Justice of the Supreme Court was given like privilege, as was the judge of any district court with relation to prisoners in jail. An act to encourage vaccination, providing for the preservation of vaccine, and extending the franking privilege for vaccine by legally authorized agents was passed by Congress in 1813 (Act February 27, 1813, ch. 37, 2 Stat. 806. Repealed in 1822). Act July 13, 1832, ch. 204, 4 Stat. 577, provided for supplementing equipment and personnel for aid in enforcement of quarantine and health laws and regulations of any state. By an act of May 26, 1866 (Res. No. 42, 14 Stat. L. 357) the Secretary of the Treasury was authorized to

"make and enforce quarantine regulations to prevent the introduction of cholera into the country."

(This authority expired in January, 1867.) By an Act of June 29, 1870, the Secretary of the Treasury was authorized to appoint a surgeon as Supervising Surgeon of the Marine Hospital Service. The first comprehensive national quarantine law enacted by the Congress was that of 1878 (April 29), "An Act to prevent the introduction of contagious or infectious diseases into the United States." It was made the duty of all medical officers of the Marine Hospital Service and customs officers to aid in the enforcement of the national rules and regulations. Also in 1878 (December 1) an appropriation was made

"for investigating the origin and causes of epidemic diseases, especially yellow fever and cholera, and the best method of preventing their introduction and spread in the United States."

An appropriation of $5,000 was made in 1879 to cover expense of "collecting data upon which to prepare bulletins of health." An Act of March 3, 1879, created a National Board of Health and specified its duties (act repealed in 1893). By an Act of May 14, 1880, the President was authorized to call an international sanitary conference

"to secure an international system of notification as to the sanitary condition of ports and places likely to be infected with yellow fever or cholera and of vessels sailing therefrom."

Financial aid to state and local boards of health and local quarantine stations was provided for in the Act of June 16, 1880, in case of epidemic. A special appropriation of $200,000 was made available to the President by an Act of September 26, 1888, to be expended in aid of state and municipal boards of health, or otherwise to prevent the introduction of cholera or yellow fever, or prevent the spread within the United States, territories or District of Columbia. Provisions for the prevention of the spread of cholera, yellow fever, smallpox or plague was contained in an Act of March 27, 1890. Additional powers and duties in relation to quarantine were provided in Acts of February 15, 1893, March 2, 1899, April 12, 1900, April 30, 1900,

and March 3, 1901. By the sundry civil appropriation Act of March 3, 1901, the sum of $35,000 was made available for the erection of building and quarters "for a laboratory for the investigation of infectious and contagious diseases and matters pertaining to the public health." (The Hygienic Laboratory, now the National Institute of Health of the Public Health Service, was actually established in 1887 by Kinyoun.) The Surgeon General's Conference of today was first provided for by an Act of Congress July 1, 1902; collection, compilation and publication of vital statistics were also provided for in this Act. By the same Congress regulation of viruses, antitoxins, etc., began. Investigation of leprosy, with special reference to Hawaii, was provided by act of June 19, 1906. Investigation as to the prevalence of tuberculosis, trachoma, smallpox and other communicable diseases among the Indians was provided for by Act of Congress in 1912, and in 1914 for a study of pellagra; rural sanitation in 1916, and for a leprosarium in 1917. An Act of 1922 established a Division of Venereal Diseases in the United States Public Health Service.

The foregoing recites, briefly, some of the Federal enactments under which national health service has been provided. Time will not permit a similar review of state laws. It may be stated that all states have some form of legally constituted health authorities and more or less adequate laws, but not more than half the counties in the United States have adequate local health services.

To employ a present popular word, we are now in a "recession" with respect to pestilence: no yellow fever, no cholera, no human plague, no epidemic smallpox, relatively little typhoid, no widespread epidemic of scarlet fever, diphtheria or other acute diseases.

It was formerly considered that war and pestilence were the only means of obviating overpopulation, but we have with us the high speed automobiles and low speed roads, heart diseases, cancer and syphilis.

In giving consideration to the progress made in the prevention of known diseases, let us not forget the work of the research scientists in bringing to light new diseases and advanced epidemiology. There are: Rocky Mountain spotted fever (Western type, carried by *Dermacentor andersoni,* Eastern type by *Dermacentor variabilis*); typhus (old world type transmitted by *P. humanus,* endemic type by *Xenopsylla cheopis*); tularemia, transmitted by *Chrysops discalis, Dermacentor andersoni,* to mention only a few of the diseases in which the epidemiologist has played his part.

Theobald Smith, in his work on Texas cattle fever, opened up the whole field of medical entomology in America. Goldberger's work on the cause, prevention and cure of pellagra is one of the high points in American public health research, likewise the work of Stiles and the Rockefeller Foundation on hookworm disease. Carter and von Ezdorf and their associates inaugurated scientific investigations of malaria prevalence in the United States and directed the first organized efforts at control through anti-anopheles measures. Lumsden may be called the "father of rural sanitation." Great credit is due the Rockefeller Foundation for the scientific work of the International Health Division in assistance in the development of sound public health practices in this country. Special attention should be called to our modern quarantine practice which guards the country from imported pestilence; to the advancement in industrial hygiene, food (particularly milk and shell-fish) sanitation, and not least, to coordination of Federal, state and local health organizations functioning with that major part of the profession, those engaged in the curative branch of medicine.

In all of our progress we are prone to forget or pass as a "matter of course" steps, at times slow, faltering and even painful or death-dealing, which brought us to our present situation. Let us here pay reverent tribute to such men as our own Carter (of extrinsic incubation period fame), Finlay, Nott, Reed, Carroll, Lazear and Agramonte; Guiteras, Murray, Theobold Smith, Ricketts, Gorgas, Goldberger, Kinyoun, Sedgwick, Whipple, Welch, Biggs, Chapin and Flexner, and to others constituting the army of martyrs and heroes of the medical profession, state and local health boards, who through their noblest efforts in periods of darkness, held the torch in public health progression.

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EDITORIAL DEPARTMENT

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SULFANILAMIDE

When Ehrlich first introduced salvarsan for syphilis nearly thirty years ago, there was an outburst of clinical papers on this preparation, many of which condemned it entirely as useless or blamed it for the development of serious complications of the disease.

It would seem that sulfanilamide as a specific for another venereal disease, gonorrhea, has swept the scientific world much more uniformly; there has been less dispute as to its effectiveness; and it is establishing itself now without real opposition. Though many clinical reports have dealt with its toxicity, none has been seen which denied that it benefits the majority of cases of gonococcal disease more than any drug hitherto tried. Questions now agitated are, not whether sulfanilamide inhibits Neisserian infection, which is apparently no longer open to debate, but why all investigators report some failures, usually in the neighborhood of 15 per cent; and the possibility of improving the compound to eliminate toxic effects and provide still more powerful antibacterial activity.

The program of the Association's New Orleans meeting last November-December devoted more space to the clinical use of sulfanilamide than to any other single therapeutic agent. In the Section on Urology an excellent symposium was presented on its activity in genito-urinary infections, which is published in this issue of the JOURNAL beginning on page 387.

Experiences well worthy of study are reported by Clark and Branham,[1] Ainsworth,[2] and Alyea, Daniel and Harris,[3] from three Southern states, Oklahoma, Mississippi, and North Carolina.

One of the explanations offered for the failure of sulfanilamide in a considerable group of cases is the fact that a portion of the drug, possibly larger in some individuals than in others, is converted to an inactive form. Since normally most of it is excreted by the kidneys unchanged, it has been suggested that its excretion offers an excellent kidney functional test. But about one-fifth is regularly changed in the body to an inactive compound, acetyl sulfanilamide, which also appears in the urine. According to Harris and Klein,[4] of Durham, if slices of rabbit liver are incubated in a test tube with sulfanilamide, a large part of the drug is acetylated, that is, changed to the inactive form found in human urine. Other rabbit tissues, as kidney and muscle, do not induce this change. Possibly in human beings, it is the liver which is responsible for conversion of the microbe-destroying form of sulfanilamide to the bacterially inert substance. That this occurs to a larger degree in persons not benefited by therapy, however, has not been demonstrated.

Sulfanilamide is, of course, the established medicament, but continued investigation of related substances shows that improvement is still to be hoped. Alyea, Daniel and Harris[3] note that two patients who failed to improve on sulfanilamide subsequently were cured by treatment with disulfanilamide. Schaeffer,[5] of Philadelphia, compared the activity of several sulfuramide compounds in a fatal hemolytic streptococcus infection of rabbits. He reports that a more complex product, phenylalanine sulfonamide, was notably better than sulfanilamide it-

1. Clark, Anson L.; and Branham, D. W.: Sulfanilamide in the Treatment of Genito-Urinary Infections. Sou. Med. Jour., **31**: 387 (April) 1938.

2. Ainsworth, Temple: Sulfanilamide in the Treatment of Gonococcic Infections in the Male. Sou. Med. Jour., **31**:391 (April) 1938.

3. Alyea, Edwin P.; Daniel, Walter E.; and Harris, Jerome S.: Sulfanilamide Therapy in Gonorrhea and Its Complications. Sou. Med. Jour., **31**:395 (April) 1938.

4. Harris, J. S.; and Klein, J. R.: Acetylation of Sulfanilamide by Liver Tissue in Vitro. Proc. Soc. Exp. Biol. & Med., **38**:78 (Feb.) 1938.

5. Schaeffer: Protective Effects Against Lethal Streptococcus Hemolyticus of Glutamine and Various Sulfonamide Compounds. Ibid, **37**:648 (Jan.) 1938.

self or several other substances studied in this disease. One hundred per cent of his animals recovered after treatment with phenylalanine sulfonamide; 75 per cent recovered after sulfanilamide; and all controls died. The more effective compound was in this case also less toxic. Hill and Goodwin,[6] of Thomasville, Georgia, report successful use of "prontylin," a sulfuramide product with three benzene rings, in the treatment of human malaria, and preference for this drug rather than sulfanilamide.

This is not to suggest that other preparations be loosely prescribed for human genito-urinary infections. Clinical experimentation is dangerous except in quarters well equipped for research. The reports merely emphasize the fact that the practitioner must keep up with the constantly changing literature of this important subject. The discomforting effects of sulfanilamide upon the patient serve a useful purpose at the moment, since they should act as a deterrent to self-medication.

CANCER AND VITAMIN A

Histology, or the study of the appearance of cells, began with the microscope and thus considerably antedated the study of the cell's chemical make-up. Knowledge of the indefinite number of chemical and physical changes which accompany alterations in the shape or function of living tissue has been slowly acquired and has been extended by ingenious combinations of analytic methods from several of the fundamental sciences.

Vitamin A, which is an essential part of the body structure, is abundant in the mitochondria of the living cell, that is, in minute rods and granules in the cytoplasm which are demonstrated by certain staining methods. These small structures may be separated from the rest of the cell by centrifuging cell suspensions at particular speeds and by suitable washing methods. The mitochondria may then, after isolation, be analyzed for vitamin A. Mitochondria of the normal liver cells are rich in this accessory food factor, even after starvation of experimental animals or after the extensive fatty changes in the liver which are seen in phosphorus poisoning. Liver of various animals is a valuable food because it stores considerable quantities of several of the known vitamins and probably of accessory foods which are still to be identified. It maintains its supply of vitamin A in the face of considerable difficulty.

Certain coal tar products are well known to stimulate the growth of carcinoma, both human and experimental. One of these, dibenzanthracene, on injection into normal rabbits, as an early effect before cancer has developed, reduces the vitamin A content of the mitochondria of normal liver cells.[1] Even if large amounts of vitamin A are injected into the animal at the same time, the liver is unable to fulfill its normal function of vitamin A storage.

It was thought possible by Goerner and Goerner,[2] of Long Island Medical College, that malignant growths might similarly prevent the storage of vitamin A in the liver of the host: that during their development they might affect the animal's liver in the same way as injections of the coal tar irritant. To investigate this problem, they therefore transplanted two different types of malignant growth, a carcinoma and a sarcoma, into a number of rabbits. The liver of the animals continued to store vitamin A, even when the tumors were quite large, and after considerable weight loss. Malignant tumors thus did not cause the particular toxic effect which dibenzanthracene had upon the liver. The mitochondria of the tumor cells themselves were examined for vitamin A and for their fatty content, and it was found that in spite of having an abundance of lipid they contained no vitamin A.

This would seem to be a characteristic abnormality of these two types of lawless growth, the particular carcinoma and the sarcoma, which differentiates them from normal tissue: neither of the two malignant tumors stored any vitamin A. The cells of both multiplied profusely without this factor.

CAUSE OF MENTAL SYMPTOMS

An amusing write-up was seen in the newspaper a few months ago of some neurotic pigs. Healthy swine had been trained by a psychologist at the ringing of a bell to make their way through a maze to a concealed trough, open the lid, and there find a large and delicious apple, which they were permitted immediately to consume. After the lesson was perfectly learned and they had many times been rewarded with the eatable, they were suddenly and unexpect-

6. Hill, R. A.; and Goodwin, M. H., Jr.: Prontosil in the Treatment of Malaria: Report of 100 Cases. Sou. Med. Jour., **30**: 1170, 1937.

1. Goerner, Alfred: Effect of Dibenzanthracene on Vitamin A and Total Lipid of Mitochondria. Jour. Biol. Chem., **122**:529 (Jan.) 1938.

2. Goerner, A.; and Goerner, M. M.: Vitamin A and Tumor Mitochondria. Ibid, **123**:57 (March) 1938.

edly given, when they opened the lid, a painful beating instead of the delicacy. The next time they went uneasily through the accustomed efforts they received the apple; at other times the drubbing, and so on irregularly, so that just as in life there was no way of predicting whether good behavior would bring them a valued prize or whether a severe punishment would follow their virtuous act. They lost appetite and weight and became quite ill. When the bell rang they lay twitching, miserable and undecided, sometimes the front legs trying to carry them forward and the hind legs moving in the opposite direction, with the typical symptoms of an advanced neurosis.

Thorner,[1] of the University of Pennsylvania, who has attempted to analyze the mind of catatonics by studying their reactions under the influence of a barbiturate, says that the condition common to all patients is indecision. They are unable to make a choice between two lines of action. This is the only factor observed in every case.

Psychiatry in recent years has stressed the objective abnormalities of the patient, and many useful innovations in therapy have resulted. The newly emphasized fact that pellagrins commonly are mental cases and that pellagra is a vitamin deficiency disease;[2] the response of certain types of dementia to hypoglycemic treatment; the mental aberrations of thyroid patients, all ably support the conception of the physical and chemical basis of psychiatric disease and its remediability with drugs.

However, purely mental treatment has a logical and even a constantly widening experimental basis. The world cannot be made just and reasonable, but the parent can help the child and the physician the patient at times, by encouraging confidence and the habit of quick decision. This is the simplest form of mental hygiene.

TWENTY-FIVE YEARS AGO

From Journals of 1913

Federal Public Health Agencies.[3]—"There can be but one opinion among thinking men as to the desirability and even necessity of a unification and extension of all national health agencies designed to conserve and promote the national health. * * * Founded by an act of Congress in 1798 as a bureau of the Treasury Department, this service [Public Health] was originally known as the Marine Hospital Service and had for its function of the medical relief of American merchant seamen and the maintenance of marine hospitals for their care. It has kept this function for 114 years, but in addition many new and important functions have been added."

Endocrinology.[4]—"The entire question of internal secretion is still in its infancy, was practically unknown only a few years ago. * * * Yet a capable physician of mature experience * * * told me a month ago that he considered that the entire future of medicine lay in the skillful administration of organic extracts! What, then, were our masters—mere charlatans?"

Endocrines in Dementia Precox.[5]—"During the last four years there have been studied in the Philadelphia General Hospital a large number of cases of dementia precox in reference to the ductless glands. * * * Of these cases eight have come to autopsy. * * * All of these cases died of tuberculosis. * * * It is a rather remarkable fact that the almost universal cause of death in dementia precox is tuberculosis, and if feebleness of resistance to the tubercle bacillus is due to the inadequacy of the adrenal system, we have reason to infer that this inadequacy pre-existed and that it is one of the factors in the make-up of dementia precox. * * *"

Incidence of Pellagra.[6]—"In his first work on insanity in 1883, Professor Spitzka states: 'Pellagrous insanity will not be discussed in this volume, as it does not occur in America and is limited to such countries as Italy, where maize forms a staple article of diet.' * * * in 1911 there were cases of pellagra diagnosed in the State of South Carolina alone to the number of 2,100. * * * It was supposed that the New England states were immune to the disease, but in the summer of 1910 several cases were reported from Rhode Island. * * * At present one authority is rather emphatic in the statement that the majority of the people in the South are suffering from some form of corn poisoning. * * * Since some form of mental aberration usually accompanies the disturbance, it is probably better known to the neurologist and the psychiatrist."

1. Thorner, M. W.: Psychologic Structure of Catatonia. A Pharmacologic Survey. Arch. Neurol. & Psychiat., **39**:512 (March) 1938.

2. Editorial. Nicotinic Acid in Pellagra. Sou. Med. Jour., **31**:331 (March) 1938.

3. Editorial. New Health Department or Present Bureau? Boston Med. & Surg. Jour., **168**:175, 1913.

4. Paris Letter. Ibid, p. 70.

5. Dercum, F. X.; and Ellis, A. G.: An Examination of the Ductless Glands in Dementia Precox. Ibid, p. 95.

6. Cohoon, E. H.; and Farnell, F. J.: Pellagra, with Report of a Case. Ibid, p. 50.

Oklahoma City — Where We Meet

OKLAHOMA CITY*

While Oklahoma is a new state, and Oklahoma City a new city, as states and cities are rated in the thinking of the American people, the Southern Medical Association's convention city for 1938 is by no means new to the convention business. Through the intelligent and efficient handling given to convention solicitation by the Oklahoma City Chamber of Commerce and its

*Prepared by the Publicity Department of the Oklahoma City Chamber of Commerce for the Southern Medical Journal.

Conventions Division, that city has become not lower than fourth in the United States, and in many recent years third, in the number of conventions entertained annually.

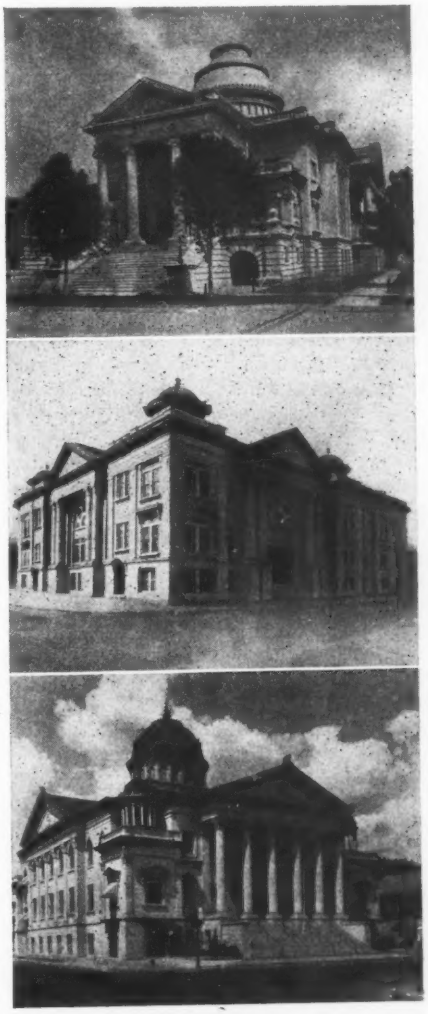
This is not an idle claim of over-enthusiastic town boosters. It is supported by reference to "World Convention Dates," New York publication, which lists and announces all conventions held in the country, and is relied upon by hotels and other institutions concerned with the number and size of conventions and when and where they are held.

For several years convention bookings announced by this medium, have shown New York first, Chicago second and Oklahoma City third. In 1936, Dallas, Texas, and Memphis, Tennessee, ranked third and fourth, respectively, due to extraordinary gatherings in those two cities, but even in those years Oklahoma City ranked third in total convention attendance. These facts are submitted in order that Southern Medical Association members may know that in planning to go to Oklahoma City this year they are justified in anticipating not only a spirit of hospitality in keeping with that to which they are accustomed, but efficiency of service in all respects comparable with the best they have had anywhere.

During 1937, Oklahoma City entertained 687 conventions having an attendance of 25 or more persons from outside the city. The record shows aggregate attendance at these gatherings to have been 176,120. Evidence already is conclusive that 1938 will see this record far surpassed. A convention already has been held in Oklahoma City this year with attendance exceeding 15,000 persons.

Last year's Southern convention was held in "America's Most Interesting City," a claim which many will hold to be justified by what New Orleans has to offer visitors, but Oklahoma City also is distinctive in several respects which will prove of much interest to Southern Medical convention delegates. It is in an oil field eleven miles long. More than one-third of the 1,600 derricks are within the city limits, many of these in unbelievable proximity to residences of high type according to any city's standards. The answer is that encroachment of the oil development upon these sections of the city has been voted by the citizen body as a whole, one relatively small zone after another being included both on the plea and over the protest of residents therein. Invasion of the down town business district was halted notwithstanding definite indication that within the proscribed district, if wells were then permitted, would be brought in some of the largest producers in the entire oil area.

Beautification of the grounds about the State Capitol building, by planting of trees, cultivation of flowers and shrubs and the landscaping



Top--St. Luke's Methodist Episcopal Church, South
Center--First Presbyterian Church
Bottom--First Christian Church

It is believed that within a radius of one-half mile from these churches more persons are engaged in public worship each Sunday morning than within any other equal area in the United States.

of park areas is going forward according to a definite plan, with black gold producers in action right in the midst of the improvement, the most paradoxical picture for visitors offered by any American city today.

Robinson Avenue, bisecting the city from north to south, has many of its best intersections marked by beautiful churches, at least six of which have memberships of from 3,000 to 5,000. It is claimed by the Religious Activities Committee of the Oklahoma City Chamber of Commerce, this committee itself a novelty in Chambers of Commerce of the nation, that there are, each Sunday morning, more persons engaged in public worship within a radius of a half mile of the corner of Eighth and Robinson in Oklahoma City, than within any other equal area in the United States, a claim which few who drive on Robinson Avenue between 10:00 a.m. and 1:00 p.m. on any Sunday will question. From Fourth to Twelfth Streets, inclusive, these Robinson Avenue churches are: First Methodist, St. John's Cathedral (Episcopalian), St. Luke's Methodist Episcopal South, First Presbyterian, First Christian, First Baptist, Temple B'Nai Israel, First Christian Science and First English Lutheran.

Pre-Dawn Easter and Pre-Christmas Pageants have become traditional in the religious life of Oklahoma City. The Easter Pageant is given in the Lincoln Park Amphitheater, which seats 18,000 persons. On Easter morning in 1937, which was March 28, 15,000 persons sat throughout the service, with temperature at 20 degrees. The Christmas Pageant is held in the Municipal Auditorium.

Further information of interest concerning life and institutions of Oklahoma City will be given in future issues of the *Journal* before the 1938 convention.

Book Reviews

Diseases of the Blood and Atlas of Hematology, with Clinical and Hematologic Descriptions of the Blood Diseases, Including a Section on Technic and Terminology. By Roy R. Kracke, M.D., Professor of Bacteriology, Pathology and Laboratory Diagnosis, Emory University School of Medicine, and Hortense Elton Garver, M.S., Instructor in Laboratory Diagnosis, Emory University School of Medicine. 531 pages, illustrated. Philadelphia: J. B. Lippincott, 1937. $15.00.

Diseases of the blood are of great importance, for not only does this tissue suffer from its own intrinsic disturbances, but it reflects more or less actively and precisely the disturbances occurring in the other organs and organ systems of the body. Increasing recognition of this key position has led during recent years to a great volume of observational and experimental work. To meet the need for collection and interpretation of such investigations reported from many clinics and laboratories there have appeared a number of textbooks of hematology. Of these none is so satisfactory as the present volume. Dr. Kracke is not only a collector and interpreter of the work of others, but an original observer and investigator whose own work has won a place in any textbook. He is gifted also with a facility for clear expression and simple straightforward presentation of facts and opinions. The book reflects these qualities.

Section 1 discusses general principles and terminology. It includes a glossary and the proposal of certain new terms which are, however, not insisted upon in the body of the book. The second section is a formal description of the blood cells. Written from the standpoint of a "trialist," it presents an impartial consideration of the prevalent theories of blood cell origin and a clear description of the characters identifying the various cell types. It embodies a series of the colored plates that are a distinguishing feature of the book. Continuing throughout the remaining sections wherever there is need for clear picturization, these plates done by the co-author are excellent not only for their careful workmanship, but also for their faithful color reproduction. As indicated in the title, they make of the book a valuable "atlas" of hematology as well as a descriptive text.

Section 3 establishes the normal standard for the leukocytes and discusses their numerical variations. In the chapter on the leukopenic diseases the author speaks with particular authority. Section 4, longest of the book, considers the various types of anemia, their causation, clinical signs and symptoms, laboratory findings, pathology, treatment and prognosis. Section 5 treats in similar manner the leukemias, and Section 6 the important group of hemorrhagic diseases. Section 7 covers infectious mononucleosis, polycythemia vera, the cytology of the bone marrow, the blood picture of laboratory animals, and chapters by collaborators on malaria and on blood groups and transfusion. There is a very complete final section on the technic of blood examination.

This book can be recommended to all who are interested in the problem of the blood and its diseases whether they be technician, medical student or physician. For each it will have its special appeal. The wealth of color plates adds to its cost, but greatly more to its value, and the excellent presswork contributes its part to the general sense of clarity and balance in the text.

Workbook in Elementary Diagnosis for Teaching Clinical History Recording and Physical Diagnosis. By Logan Clendening, Professor of Clinical Medicine, University of Kansas. 167 pages, illustrated. St. Louis: The C. V. Mosby Company, 1938. Cloth $1.50.

As the title implies, this book is intended for the sophomore medical student's use in the course of physical (elementary) diagnosis. A skeletal outline is given for the student to follow in taking the history and making the physical examination. The need for a routine method of procedure to insure completeness is emphasized.

The author describes briefly but clearly how to examine the different parts and systems of the body.

Methods of inspection, palpation, percussion and auscultation are described and many of these procedures are depicted beautifully in pen and ink drawings.

One of the features of the book is the clear description of the normal and pathological sounds heard in auscultation of the heart and lungs. Enough medical history is included to stimulate the student along this line of reading.

A very brief account of the examination of the excretions, secretions and the blood is given.

About half of the book is given over to exercises in outline form for the student to use in taking the history, doing the physical examination, correlating his findings, and suggestions for arriving at a diagnosis. Throughout the book the author stresses the importance of the student's developing his ability to find out as much as possible about the patient without the aid of mechanical diagnostic equipment.

It is a combination notebook, text and reference for the teacher and student.

Report of the Committee on Tuberculosis Among Negroes. A Five-Year Study and What it has Accomplished. 77 pages. New York: National Tuberculosis Association, 1937.

Tuberculosis, as a cause of death, ranks seventh among whites and second among Negroes. Present tuberculosis mortality among Negroes about equals the white mortality of twenty-five years ago. For Northern states the colored mortality is more than five times the white; in the Southern states the ratio is less than three.

It is concluded that, while the Negro probably has a racial handicap in his fight against tuberculosis, the disease is one of poverty "and the Negro labors under a severe environmental handicap, largely economic."

The major part of the report is devoted to measures for the control of tuberculosis among Negroes. Health education is stressed. The participation of colored physicians and colored public health nurses in a general program is recognized as important.

Tuberculosis control activities should be compiled by color and "allocation of services should be on the basis of unit need (per 100 annual deaths) and not per unit population."

The Negro's Struggle for Survival: A Study in Human Ecology. By S. J. Holmes, Professor of Zoology in the University of California. 296 pages. Berkeley, California: University of California Press, 1937. Cloth $3.00.

This is a most interesting little volume written by a true scientist who refuses to flinch from discussing the most serious perplexing problems, but, being a scientist, he declines to assume the role of prophet. He reminds us that there are four ways only for the "racial struggle to work out." (1) We shall all become black; (2) we shall all become white; (3) whites and blacks may fuse into a hybrid stock; and (4) we shall become permanently biracial either mingled together or occupying different local areas.

He discusses at great length these various possibilities. His viewpoint is objective, tolerant, unbiased and the reader is arrested on nearly every page with some unexpected fact or suggestion. Nothing is more surprising than the frank statement that any general control of venereal infections will greatly augment the Negroes' survival value. The present popularity of birth control has not greatly impaired the Negro's birth rate, but is already a serious handicap for the whites. The restriction of immigration has definitely increased the fecundity of the blacks.

This is a book that should be read, even studied by legislators, social workers, teachers and physicians. The writer has no pet hobby, no mental impressions to put over. He faces facts and asks the reader for an interpretation.

Maternal Deaths—The Ways to Prevention. By Iago Galdston, M.S., Secretary, Medical Information Bureau of the New York Academy of Medicine. 115 pages. New York: The Commonwealth Fund, 1937. Cloth $.75. Paper $.50.

This book represents a clear and impassionate discussion of the causes and prevention of maternal deaths. It is very largely based on experiences in New York City as reported in the three-year study made by the New York Academy of Medicine in 1933.

For most readers, however, the book will prove more valuable than the original report; involved statistical and technical discussions are avoided. Intended for laymen, health workers, and physicians, it can be read with profit by anyone interested in the problems of maternal mortality.

The responsibility of physicians, patients, and communities toward preventing needless loss of life are clearly stated in a manner which can create no prejudice. Of considerable value is the chapter on "What Can Be Done," which outlines the many approaches necessary for solution of the problems.

Southern Medical News

ALABAMA

The Alabama Medical Technicians' Association will hold its second annual convention in Birmingham, May 4, with headquarters at the Tutwiler Hotel. The main features of the meeting are lectures and exhibits on practical laboratory procedures, election of officers and the banquet.

The following were appointed to the five-member Board of Medical Technicians Examiners to supervise examination and registration of medical technicians in Alabama: Dr. Lloyd Noland, Fairfield, Physician member, three years; Dr. G. S. Graham, Birmingham, Physician-Pathologist, three years; Mrs. Ivy T. McBride, T. C. I. Hospital, Fairfield; Mr. Cooper Broughten, State Health Department, Montgomery; and Mrs. Elizabeth Littlepage, Sheffield, medical technician members.

Deaths

Dr. David Finis Gaston, Gastonburg, aged 77, died November 4.

Dr. William Porter Hughes, Florence, aged 70, died February 14.

Dr. John Randolph Sherman, Phil Campbell, aged 65, died November 8 of arteriosclerosis and chronic heart disease.

ARKANSAS

Ashley County Medical Society has elected the following officers: Dr. J. T. Wood, Crossett, President, and Dr. W. C. Riggins, Hamburg, Secretary.

Carroll County Medical Society has elected the following officers: Dr. C. W. Slusser, Green Forest, President; Dr. J. F. John, Eureka Springs, Vice-President; and Dr. D. J. McCurry, Green Forest, Secretary-Treasurer.

Chicot County Medical Society has elected the following officers: Dr. W. D. Easterling, President; Dr. J. H. Burge, Vice-President; and Dr. W. J. Schwarz, Secretary-Treasurer, all of Lake Village.

Clark County Medical Society has elected the following offi-

cers: Dr. H. A. Ross, Arkadelphia, President; and Dr. Joe W. Reid, Arkadelphia, Secretary-Treasurer.

Clay County Medical Society has elected the following officers: Dr. O. B. Clopton, Rector, President; Dr. J. B. Futrell, Rector, Vice-President; and Dr. J. E. McGuire, Piggot, Secretary-Treasurer.

Desha County Medical Society has elected the following officers: Dr. J. H. Hellums, Dumas, President, and Dr. H. T. Smith, McGehee, Secretary-Treasurer.

Drew County Medical Society has elected the following officers: Dr. J. S. Wilson, Monticello, President; Dr. J. P. Price, Jr., Monticello, Vice-President; and Dr. Van T. Binns, Secretary-Treasurer.

Grant County Medical Society has elected the following officers: Dr. C. F. Cole, Prattsville, President, and Dr. Miles F. Kelly, Sheridan, Secretary-Treasurer.

The Hot Springs County Medical Society has elected the following officers: Dr. J. M. Norton, Donaldson, President; Dr. W. F. Barrier, Malvern, Vice-President; and Dr. W. G. Hodges, Malvern, Secretary-Treasurer.

Howard-Pike County Medical Society has elected the following officers: Dr. T. F. Alford, Murfreesboro, President; Dr. J. S. Hopkins, Nashville, Vice-President; and Dr. H. H. Holt, Nashville, Secretary-Treasurer.

Lee County Medical Society has elected the following officers: Dr. H. L. White, Rondo, President, and Dr. N. C. Hodge, Marianna, Secretary-Treasurer.

Miller County Medical Society has elected the following officers: Dr. W. D. Smith, Texarkana, President; Dr. W. H. Daubs, Lewisville, Vice-President; and Dr. N. B. Daniel, Texarkana, Secretary-Treasurer.

Nevada County Medical Society has eleced the following officers: Dr. A. S. Buchanan, Prescott, President; Dr. J. B. Hesterly, Prescott, Vice-President; and Dr. R. P. Hughes, Okolona, Secretary-Treasurer.

Phillips County Medical Society has elected the following officers: Dr. Morriss Henry, Helena, President; Dr. W. A. Ellis, Helena, Vice-President; and Dr. H. H. Rightor, Helena, Secretary-Treasurer.

Pope-Yell County Medical Society has elected the following officers: Dr. R. L. Smith, Russellville, President; Dr. Walter Cale, Atkins, Vice-President; and Dr. Roy I. Millard, Dardanelle, Secretary-Treasurer.

Union County Medical Society has elected the following officers: Dr. W. S. Riley, El Dorado, President; Dr. J. K. Sheppard, El Dorado, Vice-President; and Dr. H. J. Mayfield, Secretary-Treasurer.

White County Medical Society has elected the following officers: Dr. S. J. Allbright, Searcy, President; Dr. C. M. Peeler, Pangburn, Vice-President; and Dr. A. J. Dunklin, Searcy, Secretary-Treasurer.

The staff of Saint Vincent's Infirmary, Little Rock, has elected the following officers: Dr. D. A. Rhinehart, President; Dr. Paul L. Mahoney, Vice-President; and Dr. Hoyt R. Allen, Secretary-Treasurer.

Dr. Max McAllister has been assigned as Health Officer for Benton County.

Dr. Elizabeth Fletcher, Little Rock, has been appointed Psychiatrist to the Pulaski County Juvenile Court.

Dr. James M. Kolb has returned to active practice at Clarksville after being on duty with CCC Camps for the past two years.

Dr. Val Parmley, Little Rock, has been reappointed Chairman of the Southern Section of the American Congress of Physical Therapy. He has also been appointed Director of the crippled children's division of the State Department of Public Welfare.

Dr. E. H. White, Little Rock, has been appointed Professor of Obstetrics in the University of Arkansas School of Medicine.

Dr. J. B. Jameson is constructing a medical building at Camden.

Dr. J. N. Compton, Little Rock, has been elected a Fellow of the American College of Physicians.

Dr. Frank Vinsonhaler has been elected President of the Little Rock Columbia University Alumni.

Dr. Raymond C. Cook and Miss Mary Eleanor Sims, both of Little Rock, were married February 9.

Deaths

Dr. George Homer Buffington, Decatur, aged 69, died January 24 of heart disease.

Dr. George F. Jackson, Little Rock, aged 49, died January 25 of heart disease.

Dr. Fleming James O'Connor, Little Rock, aged 53, died February 3 of a heart attack.

Dr. Charles Edward Robinson, Little Rock, aged 84, died November 16 of uremia and chronic nephritis.

Dr. William W. York, Ashdown, aged 63, died February 3 of injuries sustained in an automobile accident.

DISTRICT OF COLUMBIA

The Third International Goiter Conference will be held in Washington, September 12-14. The Secretary is Dr. William Blair Mosser, Kane, Pennsylvania, and the Program Chairman is Dr. Allen Graham, 2020 East Ninety-Third Street, Cleveland, Ohio.

Assistant Surgeon General Robert Olesen will direct a survey of Washington's health problems, launched by the U. S. Public Health Service at the request of the Commissioners of the District.

Dr. James M. Suter, Washington, has been appointed Health Officer of Lee County.

Dr. Williams W. Fuller, Christiansburg, has been appointed Health Officer of Montgomery County.

Dr. A. L. Tynes, Jr., Captain, M. C., U. S. Army, having recently returned from Panama, has been assigned to duty at the Walter Reed General Hospital, Washington.

Dr. Perceval S. Rossiter, Surgeon General of the U. S. Navy, and Capt. Harold Wellington Smith, in charge of the Naval Medical School, Washington, have been promoted to the rank of Rear Admiral in the Naval Medical Corps.

Deaths

Dr. Albert Watkins Evans, Washington, aged 67, died November 7 of carcinoma of the cecum.

Dr. Cary Travers Grayson, Washington, aged 59, died February 15.

FLORIDA

Alachua County Medical Society has elected the following officers: Dr. Thomas A. Snow, Gainesville, President; Dr. J. E. Maines, Sr., Lake Butler, Vice-President; and Dr. H. M. Merchant, Gainesville, Secretary-Treasurer.

Bay County Medical Society has elected the following officers: Dr. W. J. Blackshear, Panama City, President; Dr. Don S. Fraser, Panama City, Vice-President; and Dr. W. C. Roberts, Panama City, Secretary-Treasurer.

Brevard County Medical Society has elected the following officers: Dr. G. E. Christie, Titusville, President; Dr. W. J. Creel, Eau Gallie, Vice-President; and Dr. I. K. Hicks, Melbourne, Secretary-Treasurer.

Columbia County Medical Society has elected the following officers: Dr. W. S. Nichols, Lake City, President; Dr. W. M. Ives, Lake City, Vice-President; and Dr. H. S. Howell, Lake City, Secretary-Treasurer.

Marion County Medical Society has elected the following officers: Dr. Carney W. Mimms, Ocala, President; Dr. Edwin C. Hanson, Belleview, Vice-President; and Dr. R. C. Cumming, Ocala, Secretary-Treasurer.

Pasco-Hernando-Citrus County Medical Society has elected the following officers: Dr. S. C. Harvard, Brooksville, President; Dr. William Haywood Walters, Vice-President, Pasco County; Dr. Claude Carter, Vice-President, Citrus County; and Dr. G. R. Creekmore, Brooksville, Secretary-Treasurer.

St. Johns County Medical Society has elected the following officers: Dr. John J. Spencer, St. Augustine, President; Dr. G. Walter Potter, St. Augustine, Vice-President; and Dr. Vernon A. Lockwood, St. Augustine, Secretary.

The medical staff of St. Luke's Hospital, Jacksonville, has elected the following officers: Dr. Stanley Erwin, President; Dr. Ferdinand Richards, Vice-President; and Dr. William S. Manning, Secretary.

Dr. Benjamin A. Chapman, Jacksonville, has been appointed a member of the State Board of Medical Examiners, succeeding the late Dr. John M. Mann.

Dr. Thomas Dwight Sloan, formerly Superintendent of the New York Postgraduate Medical School and Hospital, has been appointed Superintendent of the Flagler Hospital, St. Augustine.

Dr. Fred Mathers has opened offices at 323 Exchange Building, Orlando, for the practice of internal medicine.

Dr. J. J. Guerra has opened offices in the First National Bank Building, Tampa. He has been connected with the Vinson Urological Clinic.

Dr. William S. Nichols, Lake City, has been appointed State Ophthalmologist by the State Welfare Board.

Dr. Lucien Y. Dyrenforth, Jacksonville, recently received a certificate in Clinical Pathology and Pathologic Anatomy from the American Board of Pathology.

Continued on page 34

An after hours talk about Balanced Radiography

BY DR. "X" AND DR. "Z"

DOCTOR X—"What is this I hear about Balanced Radiography?"

DOCTOR Z—"Oh yes, we were talking about that last night. Balanced Radiography is a term that the Patterson Screen Company uses. I think it is a good one, too, as applied to the advantages of Intensifying Screens."

DOCTOR X—"Well, it is a term that certainly intrigues my interest. What does it mean?"

DOCTOR Z—"Simply this, that by using X-ray Intensifying Screens you bring into proper balance the various factors which the roentgenologist must deal with and control in the practice of his art."

X-RAY INTENSIFYING SCREENS ASSURE BALANCED RADIOGRAPHY

1. They greatly reduce exposure time.
2. They greatly reduce danger of movement.
3. They minimize danger of over-exposure to patients.
4. They permit larger number of repeat exposures.
5. They assure a high degree of detail and maximum contrast.
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Patterson X-ray Screens assure Balanced Radiography...plus radiographs of highest possible quality.

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Intensive Post Graduate Course In Ophthalmology

(Continuation of last year's Course)

George Washington University
School of Medicine
Washington, D. C.

For Graduates in medicine,
April 18-23rd, 1938 inclusive

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Drs. Harry S. Gradle, John Green, E. C. Ellett, Walter B. Lancaster, S. Judd Beach, J. H. Dunnington, Arthur J. Bedell, A. D. Ruedemann, John N. Evans, Frank E. Burch, Alfred Cowan, W. H. Crisp, Jonas Friedenwald, LeGrand H. Hardy, Robert Von der Heydt, Edmund B. Spaeth, S. Hanford McKee, Clyde A. Clapp, Derrick Vail.

RESIDENT MEMBERS

Drs. Wm. Thornwall Davis, Ernest Sheppard, G. Victor Simpson, E. Leonard Goodman, Ronald A. Cox, George B. Jenkins, Frank D. Costenbader, Lt. Col. J. E. Ash, MC USA, Lt. Col. Frederic H. Thorne, MC USA, Capt. Elbert DeCoursey, MC USA.

Fee $40.00

Interviews will be given by Drs. Green, Lancaster and Beach to registrants of the course regarding the examinations of the American Board of Ophthalmology. Interviews can be arranged through Miss Lea Stelzer, 6830 Waterman Ave., St. Louis.

SPECIAL THREE DAY COURSE limited to 25 participants. Fee $25.00, April 15th-17th, 1938 inclusive on Surgery, Ocular Pathology and Orthoptics.

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(a) Courses leading to advanced degrees.

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(Either of the above courses are adaptable towards satisfying certain requirements of the various specialty boards)

(c) Short intensive courses in special limited fields.

(d) Review courses intended for practicing physicians.
(Two six weeks' review courses offered each session. The first began early January and the second mid February.)

(e) Extra-mural teaching through the Extension Division.

For detailed information write (stating type of course wanted) to

DIRECTOR OF GRADUATE STUDIES
1430 Tulane Avenue New Orleans, La.

Continued from page 463

Dr. Robert M. Baker, Jacksonville, and Miss Claire Henderson, Tampa, were married December 15.

Dr. Earl Henry Diehl and Miss Ruby Clyde Cain, both of Dunedin, were married October 27.

Dr. John Douglas Ferrara and Miss Margaret McGraw, both of Jacksonville, were married January 29.

Dr. H. L. Harrell, of Dade City, and Miss Frances Allen, of Lewisburg, Tennessee, were married November 27.

DEATHS

Dr. L. M. Anderson, Lake City, aged 77, died January 21.

Dr. George William Fitch, St. Petersburg, aged 71, died November 21.

Dr. W. M. Matthews, Polk City, aged 50, died November 5.

Dr. A. B. Quasser, Jacksonville, aged 42, died February 3.

Dr. John Benjamin Shelton, Dania, aged 76, died November 29.

Dr. Wilbur Fisk Yarbrough, Miccosukee, aged 71, died November 9 of chronic bronchitis.

GEORGIA

Butts County Medical Society has elected the following officers: Dr. B. F. Akin, Jackson, President, and Dr. R. L. Hammond, Jackson, Secretary-Treasurer.

Baldwin County Medical Society has elected the following officers: Dr. G. K. Cornwell, Milledgeville, President; Dr. L. A. Bailey, Milledgeville, Vice-President; and Dr. J. R. S. Mays, Milledgeville, Secretary-Treasurer.

Burke County Medical Society has elected the following officers: Dr. E. A. Bargeron, Waynesboro, President; Dr. W. C. McCarver, Vidette, Vice-President; and Dr. Abe J. Davis, Waynesboro, Secretary-Treasurer.

Chattooga County Medical Society has elected the following officers: Dr. R. E. Talley, Trion, President; Dr. H. D. Brown, Summerville, Vice-President; and Dr. Inman Smith, Trion, Secretary-Treasurer.

Clayton-Fayette Counties Medical Society has elected the following officers: Dr. J. R. Wallis, Lovejoy, President; Dr. E. C. Seawright, Fayetteville, Vice-President; and Dr. T. J. Busey, Fayetteville, Secretary-Treasurer.

Cobb County Medical Society has elected the following officers: Dr. H. B. Terry, Acworth, President; Dr. J. E. Lester, Marietta, Vice-President; and Dr. A. H. Fowler, Marietta, Secretary-Treasurer.

Emanuel County Medical Society has elected the following officers: Dr. S. S Youmans, Oak Park, President; Dr. R. G. Brown, Graymont, Vice-President; and Dr. R. C. Franklin, Swainsboro, Secretary-Treasurer.

Glynn County Medical Society has elected the following officers: Dr. M. E. Winchester, Brunswick, President; Dr. Webb Conn, Brunswick, Vice-President; and Dr. T. V. Willis, Brunswick, Secretary-Treasurer.

Hall County Medical Society has elected the following officers: Dr. E. L. Ward, New Holland, President; Dr. W. D. Cagle, Gainesville, Vice-President; and Dr. Hartwell Joiner, Gainesville, Secretary-Treasurer.

Hart County Medical Society has elected the following officers: Dr. A. O. Meredith, Hartwell, President; Dr. H. E. Teasley, Hartwell, Vice-President; and Dr. G. T. Harper, Dewy Rose, Secretary-Treasurer.

Habersham County Medical Society has elected the following officers: Dr. D. T. Rankin, Alto, President; Dr. C. T. Hardman, Tallulah Falls, Vice-President; and Dr. B. J. Roberts, Cornelia, Secretary-Treasurer.

Taylor County Medical Society has elected the following officers: Dr. S. H. Bryan, Reynolds, President; Dr. F. H. Sams, Reynolds, Vice-President; and Dr. R. C. Montgomery, Butler, Secretary-Treasurer.

Sumter County Medical Society has elected the following officers: Dr. W. F. Castellow, Americus, President; Dr. J. W. Chambliss, Americus, Vice-President; and Dr. Marion W. Hester, Americus, Secretary-Treasurer.

Tattnall County Medical Society has elected the following officers: Dr. A. C. Branch, Glennville, President; Dr. L. R. Jelks, Reidsville, Vice-President; and Dr. J. M. Hughes, Glennville, Secretary-Treasurer.

Terrell County Medical Society has elected the following officers: Dr. Guy Chappell, Dawson, President; Dr. J. C. Tidmore, Dawson, Vice-President; and Dr. Steve P. Kenyon, Dawson, Secretary-Treasurer.

Thomas County Medical Society has elected the following of-

Continued on page 35

Reproduced from a film radiograph made on

EASTMAN ULTRA-SPEED SAFETY X-RAY FILM

(See back of this page)

Excerpts from leading Medical Journals

"*You may well ask, What are we to do about it [carcinoma of the stomach]? There is one thing that can be done and that is to advocate a routine x-ray examination in all patients of forty-five years or over who do not seem to be up to par, and to repeat this examination periodically.*"—AM. J. DIGESTIVE DISEASES & NUTRITION, *4:*149, 1937

"*Perhaps there is no single diagnostic procedure [for carcinoma of the stomach] of such importance as the roentgen examination.*"—AM. J. CANCER, *27:*745, 1936

"*The importance of x-ray examination [when carcinoma of the stomach is suspected] cannot be overemphasized, the accuracy of diagnosis in all except the occasional ulcer-carcinoma being nearly 100 per cent.*"—ANN. SURG. *96:*591, 1932

The obvious excellence of the original radiograph from which the reproduction printed on the reverse side of this page was made is due, first, to the knowledge of the radiologist; second, to the use of Eastman X-ray Film.

»

REFER YOUR PATIENT TO A COMPETENT RADIOLOGIST

«

EASTMAN KODAK COMPANY

Medical Division—Rochester, N. Y.

(*See reverse side of this page*)

Continued from page 34

ficers: Dr. Roy A. Hill, Thomasville, President; Dr. T. A. Futch, Jr., Thomasville, Vice-President; and Dr. Rudolph Bell, Thomasville, Secretary-Treasurer.

Tri-County Medical Society has elected the following officers: Dr. W. O. Shepard, Bluffton, President; Dr. J. S. Beard, Edison, Vice-President; and Dr. W. H. Wall, Blakely, Secretary-Treasurer.

Troup County Medical Society has elected the following officers: Dr. S. C. Rutland, LaGrange, President; Dr. D. E. Morgan, LaGrange, Vice-President; and Dr. Kenneth D. Grace, LaGrange, Secretary-Treasurer.

Whitfield County Medical Society has elected the following officers: Dr. J. H. Steed, Dalton, President; Dr. G. L. Broaddrick, Dalton, Vice-President; and Dr. H. J. Ault, Dalton, Secretary-Treasurer.

The Johns Hopkins Alumni Association of Georgia, at its annual banquet held on February 26 in Atlanta, elected the following officers: Dr. M. T. Edgerton, President; Dr. Floyd W. McRae, Vice-President; and Dr. J. H. Kite, Secretary-Treasurer, all of Atlanta.

The newly elected officers of the Georgia Baptist Hospital staff, Atlanta, are: Dr. Olin S. Cofer, President; Dr. S. T. Brown, First Vice-President; Dr. T. P. Goodwyn, Second Vice-President; and Dr. George W. Fuller, Secretary.

The newly elected officers of the Emory University Hospital staff, Atlanta, are: Dr. Dan C. Elkin, President; Dr. M. K. Bailey, Vice-President; and Dr. Homer H. Allen, Decatur, re-elected Secretary-Treasurer.

Dr. Albert O. Linch, Atlanta, received the L. C. Fischer Award of $100.00 for the paper showing the most original work at the annual meeting of the Fulton County Medical Society in Atlanta in January. At this meeting Drs. William T. Asher, Charles E. Boynton and Marion McHenry Hull were presented with certificates of honorary membership in the County Society.

Dr. Wadley R. Glenn announces the opening of offices at 307 Doctors Building, Atlanta, with practice limited to surgery.

Dr. John L. Dorough, Monroe, has been appointed Health Commissioner of Walton County Health Unit.

Dr. H. H. McGee, Savannah, has been elected Third Vice-President of the Chatham-Savannah Tuberculosis Association.

Harvard Medical School

Courses for Graduates

SURGICAL TECHNIQUE
June 6 - 18

By Dr. Elliott C. Cutler and Dr. Robert Zollinger at the Peter Bent Brigham Hospital and Harvard Medical School, Laboratory of Surgical Research.

Intensive practical instruction in surgical technique.

Attendance limited. Fee $150.

Apply to
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Dr. Chas. J. Woods, formerly of Tulsa, Oklahoma, is now located in Macon with offices in the Georgia Casualty Building, practice limited to dermatology and use of radium.

The Adams Hospital, Cordele, built by Dr. and Mrs. Charles Adams, was formally opened in January.

The medical staff of St. Joseph's Infirmary, Atlanta, recently installed Dr. John W. Turner as President; Dr. W. L. Champion, President-Elect; Dr. B. McH. Cline, Vice-President; and Dr. Troy Bivings, Jr., Secretary-Treasurer.

Dr. Louis Holtz, formerly with Company 4488, CCC, at Ashland, Alabama, is now doing general practice at Jonesboro. He has been appointed local surgeon for the Southern Railway.

Dr. C. E. Wills, Washington, has been appointed Director of the Washington General Hospital.

DEATHS

Dr. Robert Bennett Cuthbert, Trenton, aged 71, died December 17 of ruptured peptic ulcer and peritonitis.

Dr. Elzie David Ford, Ray City, aged 62, died December 25.

Dr. James Hawkins Heflin, Atlanta, aged 64, died January 24.

Dr. Sidney Fain Hutcherson, Adairsville, aged 52, died January 12.

Dr. Otis Burgess Moye, Soperton, aged 62, died January 20.

Dr. Homer Seal McCoy, Sylvester, aged 55, was killed suddenly in an automobile accident December 21.

Dr. Samuel Barfield Palmer, Macon, aged 66, died November 5 of adenocarcinoma of the paranasal sinuses.

Dr. Marshall Ashby Purse, Saint Simons Island, aged 72, died January 8.

Dr. James Miller Smith, Valdosta, aged 62, died January 8.

Dr. Jefferson Gillum Smith, McDonough, aged 61, died February 5.

Dr. L. H. Smith, Atlanta, aged 68, died November 30 of uremia and mitral stenosis.

Dr. Edward L. Toomer, Fitzgerald, aged 55, died November 2 of cerebral hemorrhage and uremia.

KENTUCKY

The Kentucky State Medical Association will hold its next annual meeting at the Brown Hotel, Louisville, October 3-6.

Boyle County Medical Society has elected the following officers: Dr. D. M. Godbey, Perryville, President; Dr. S. B. Sharpe, Vice-President; and Dr. P. C. Sanders, Danville, Secretary-Treasurer.

On May 5, 1937, a group of psychiatrists practicing in Kentucky met in Lexington for the purpose of organizing a psychiatric association. As a result of this meeting the Kentucky Psychiatric Association was formed and the following officers were elected for the year 1937-1938: Dr. Isham Kimbell, Lexington, President; Dr. Spafford Ackerly, Louisville, Vice-President; and Dr. Robert H. Felix, Lexington, Secretary-Treasurer. The first annual meeting was held in Louisville in January.

DEATHS

Dr. Benjamin T. Black, Campbellsville, aged 73, died December 30 of pneumonia.

Dr. Levy Millspaugh Hathaway, Owensboro, aged 60, died December 14.

Dr. William Lucien Heizer, Sr., Lexington, aged 57, died December 9 of coronary occlusion and nephritis.

Dr. Asa N. Jones, Walton, aged 82, died November 3.

LOUISIANA

Fifth District Medical Society has elected the following officers: Dr. W. H. Hamley, Lake Providence, President; Dr. E. O. Edgerton, Tallulah, First Vice-President; Dr. Ralph Talbot, Monroe, Second Vice-President; and Dr. R. Morgan Simonton, Monroe, Secretary-Treasurer.

Rapides Parish Medical Society has elected the following officers: Dr. D. C. McBride, Alexandria, President; Dr. I. F. Littell, Alexandria, First Vice-President; Dr. James Welch, Alexandria, Second Vice-President; and Dr. J. A. White, Jr., Alexandria, Secretary-Treasurer.

Physicians recently appointed to serve with the State Hospital Board are: Dr. James T. Nix, Chairman, and Dr. Rigney D'Aunoy, Vice-Chairman, and Dr. George S. Bel, Dr. Charles L. Brown, Dr. Joseph A. Danna, Dr. Robert A. Strong, and Dr. H. Vernon Sims, all of New Orleans.

Dr. A. J. Hockett was recently named Secretary and Dr. Shirley C. Lyons a member of the Board of the Hospital Service Association of New Orleans.

Continued on page 36

Washington University School of Medicine

Announces the following course

in

DISEASES OF THE HEART

A two weeks course for practitioners who wish to acquaint themselves with the more recent developments in the study of diseases of the heart and circulation.

The course begins May 16th, 1938. Fee for the course is $50.00.

For further information apply to

The Registrar

Washington University School of Medicine,
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Washington University School of Medicine

Announces the following course

in

OTOLARYNGOLOGY

An eight months' course in Otolaryngology for those beginning the study of diseases of the ear, nose and throat.

Only graduates of medical schools who have completed a year of intern service will be admitted to the course.

The course begins September 19, 1938. Fee for the course is $600.00.

For further information apply to

THE REGISTRAR
WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE

St. Louis, Missouri

Continued from page 35

Dr. John T. O'Ferrall, New Orleans, has been named a member of the Orthopedic Council of the National Foundation for Infantile Paralysis. This Foundation was created under the direction of President Roosevelt and will supplement the Warm Springs Foundation.

Hotel Dieu, New Orleans, has elected to its staff the following officers: Dr. A. D. Mouledoux, President; Dr. C. Grenes Cole, Vice-President; and Dr. C. E. Gorman, Secretary-Treasurer. Other members of the Board are Dr. T. T. Gately, Dr. Frank Chetta, Dr. P. A. Kibbe, Dr. Walter Otis and Dr. D. J. Murphy.

The Baptist Hospital, New Orleans, has elected to its staff the following officers: Dr. Henry B. Alsobrook, President; Dr. E. Z. Brown, Vice-President; Dr. Robert H. Potts, Secretary; and Dr. Robyn W. Hardy, Treasurer.

At the recent annual meeting of the Tuberculosis and Public Health Association of Louisiana Dr. W. H. Seemann was reelected President and Dr. W. Harvey Perkins, First Vice-President; Dr. Emile Naef was elected to the Board and Dr. Robert Strong re-elected, all of New Orleans.

Dr. Isadore Brickman has been appointed Superintendent of the State Colony and Training School at Alexandria. He has been Acting Superintendent since the resignation of Dr. Rutledge C. Tompkins on account of ill health.

Dr. F. F. Young, Physician-in-Chief of the Fenwick Sanitarium, Covington, has been appointed a member of the Advisory Committee to the State Hospital Director of Louisiana.

Dr. Roy B. Harrison, New Orleans, was honored by being selected as President of the Federation of State Medical Boards in Chicago in February.

Dr. John Conant Weed, New Orleans, and Miss Alice Lemann, Donaldsonville, were married in November.

Deaths

Dr. Hezzie Donice Bulloch, Covington, aged 53, died January 31 of coronary occlusion.

Dr. Joel Augustus Dawson, Jr., New Orleans, aged 28, died December 20.

Dr. Philip Samuel Perkins, Sulphur, aged 42, died November 29 of pneumonia.

Dr. Joseph Odess Prejean, Abbeville, aged 29, died November 2 of pulmonary tuberculosis.

Dr. R. L. Stewart, Koran, aged 59, died November 23.

MARYLAND

American Physiological Society will hold its next meeting in Baltimore, March 30-April 2.

American Society for Experimental Pathology will hold its next meeting in Baltimore, March 30-April 2.

American Society for Pharmacology and Experimental Therapeutics will hold its next meeting in Baltimore, March 30-April 2.

American Society of Biological Chemists will hold its next meeting in Baltimore, March 30-April 2.

Allegany-Garrett County Medical Society has elected the following officers: Dr. F. M. Wilson, Cumberland, President; Dr. C. D. Stiles, Frostburg, Vice-President; Dr. Joseph P. Franklin, Cumberland, Secretary; and Dr. Howard L. Tolson, Cumberland, Treasurer.

Anne Arundel County Medical Society has elected the following officers: Dr. John M. Claffy, Gambrills, President; Dr. A. L. Anderson, Annapolis, Vice-President; Dr. Maurice F. Klawans, Annapolis, Secretary; and Dr. Frances E. Weitzman, Annapolis, Treasurer.

Carroll County Medical Society has elected the following officers: Dr. S. L. Bare, DeTour, President; Dr. R. R. Diller, DeTour, Vice-President; and Dr. James T. Marsh, New Windsor, Secretary-Treasurer.

Cecil County Medical Society has elected the following officers: Dr. Winfred T. Morrison, Elkton, President; Dr. James F. Magraw, Perryville, Vice-President; and Dr. R. C. Dodson, Rising Sun, Secretary-Treasurer.

Harford County Medical Society has elected the following officers: Dr. J. H. Bay, Havre De Grace, President; Dr. W. E. Arthur, Cardiff, Vice-President; and Dr. G. C. Palmer, Secretary-Treasurer.

A graduate week in medical history will be held at the Institute of the History of Medicine, Johns Hopkins University School of Medicine, Baltimore, April 18-23. Each morning one lecture on some basic subject will be given by the Director of the Institute, Dr. Henry E. Sigerist, and members of his staff.

Continued on page 38

CONTRAST MEDIA VARY
IN EFFECTIVENESS AS STARS
VARY IN BRILLIANCE

LIPIODOL (LAFAY)
FOR PRECISE
SHARP RADIOGRAPHS

These, briefly, are the eight essential features of Lipiodol (Lafay):

1. The original French iodized oil*
2. Not a chloro-iodized oil—contains no chlorine
3. Light amber color—helps detect deterioration
4. Bland and well tolerated even by delicate tissues
5. Relatively non-irritating and non-toxic
6. Precise, clear cut, sharply outlined radiographs
7. Facilitates diagnosis of many obscure conditions
8. Reveals pathologic conditions which ordinary radiographs cannot visualize.

*Iodized Poppy-Seed Oil 40

LIPIODOL (LAFAY)

Continued from page 36

Dr. Francis F. Schwentker resigned as Director of Medical Research in the Baltimore City Health Department January 1 to study scarlet fever in Rumania under the auspices of the Rockefeller Foundation. His headquarters will be in Jassy.

Dr. T. Campbell Goodwin, Baltimore, and Dr. Mary Stewart Hooke, Poughkeepsie, New York, were married January 31.

DEATHS

Dr. William Henry Montague, Baltimore, aged 56, died November 8 of myocarditis.

MISSISSIPPI

Central Medical Society has elected the following officers: Dr. J. T. Rainer, Yazoo City, President. Vice-Presidents: Dr. A. G. Ward, Hinds County; Dr. Frank Lacey, Leake County; Dr. R. M. Seawright, Madison County; Dr. L. V. Willey, Rankin County; Dr. George Townsend, Scott County; Dr. W. J. C. Weimars, Simpson County; and Dr. H. E. Frizell, Yazoo County. Dr. Lawrence W. Long, Jackson, Secretary; and Dr. N. F. Kendall, Jackson, Treasurer.

Coahoma County Medical Society has elected the following officers: Dr. Wm. W. Warfield, Clarksdale, President; Dr. D. H. Raney, Mattson, Vice-President; and Dr. N. C. Knight, Clarksdale, Secretary-Treasurer.

DeSoto County Medical Society has reelected the officers for 1937 as follows: Dr. J. M. Wright, Hernando, President; Dr. H. M. Wadsworth, Hernando, Vice-President; and Dr. L. L. Minor, Memphis, Tennessee, Secretary-Treasurer and Editor.

East Mississippi Medical Society elected Dr. C. H. Harrison, Philadelphia, President.

The following physicians were awarded three-months fellowships to Tulane University Medical School by the Commonwealth Fund of New York City: Dr. Rufus DePriest, Houston; Dr. William J. Aycock, Calhoun City; Dr. John C. Butler, Laurel; Dr. James P. Wiggins, Cleveland; Dr. DeWitt T. Allred, Collins; Dr. Joseph S. Gatlin, Laurel; Dr. Benjamin G. Bush, Vaughan; and Dr. Dexter D. Johnson, Belmont.

The following officers of the Mississippi State Board of Health were reappointed: Dr. James W. Lipscomb, Columbus, President; Dr. Leonidas B. Austin, Rosedale, a member of the Board; and Dr. Felix J. Underwood, Jackson, executive officer.

Dr. O. A. Schmid has announced the opening of offices in Threefoot Building, Meridian, practice limited to neuropsychiatry.

Dr. C. T. Berry, Greenville, who recently conducted a clinic organized for treatment of indigent venereal cases under the sponsorship of the local Medical Society, Public Health Department and Red Cross, was awarded a scholarship for the period of one month for the study of syphilis at Vanderbilt University School of Medicine. The U. S. Public Health Service awarded the scholarship.

Dr. Lawrence L. Beall, Cleveland, has been awarded a one year's residency at the New York State Tuberculosis Sanatorium, Oneonta, New York, by the Commonwealth Fund of New York.

Dr. J. J. Pittman, Tylertown, has been appointed Health Officer of Walthal County, succeeding Dr. Lampton Crawford.

Dr. J. T. Senter, Fulton, has been appointed Health Officer of Itawamba County, succeeding to the post of the late Dr. N. W. Nanney.

The Lauderdale County Health Department has been granted a new modern health center building to be equipped with landscaped grounds, to be provided by the Commonwealth Fund of New York City. The City of Meridian will furnish the site for the building.

DEATHS

Dr. Darell Martin Busby, Phoenix, aged 53, died December 27 of cerebral hemorrhage.

Dr. James Craig Mazique, Natchez, aged 67, died December 12 of diabetes mellitus, gangrene and arteriosclerosis.

Dr. Albert Lee Monroe, Newton, aged 63, died November 11 of coronary thrombosis.

Dr. William Andrew McMahen, Union, aged 54, died November 15 of chronic nephritis and hypertension.

Dr. Thomas Edward Stafford, Vosburg, aged 65, died in November of angina pectoris.

MISSOURI

Cooper County Medical Society has elected the following officers: Dr. George W. Winn, Boonville, President; Dr. Arie C. H. Van Ravensway, Boonville, Vice-President; and Dr. J. C. Tincher, Boonville, Secretary-Treasurer.

Cole County Medical Society has elected the following officers: Dr. James G. Bruce, Jefferson City, President; Dr. W. W. Rambo, Jefferson City, Vice-President; and Dr. James A. Hill, Jefferson City, Secretary-Treasurer.

Bent County Medical Society has elected the following officers: Dr. William G. Dillon, Salem, President; Dr. John O. Ficke, Salem, Vice President; and Dr. Fred E. Butler, Salem, Secretary-Treasurer.

Greene County Medical Society has elected the following officers: Dr. A. W. Gifford, Springfield, President; Dr. Charles El Feller, Springfield, Vice-President; Dr. J. L. Johnston, Springfield, Secretary; and Dr. R. Ned White, Springfield, Treasurer.

Jasper County Medical Society has elected the following officers: Dr. B. E. DeTar, Joplin, President; Dr. R. M. James, Joplin, Vice-President; Dr. M. H. Black, Joplin, Secretary; and Dr. H. D. McGaughey, Joplin, Treasurer.

Dunklin County Medical Society has elected the following officers: Dr. John D. VanCleve, Malden, President; Dr. E. G. Cope, Hornersville, Vice-President; and Dr. T. J. Rigdon, Kennett, Secretary-Treasurer.

St. Charles County Medical Society has elected the following officers: Dr. A. P. Erich Schulz, St. Charles, President; Dr. George E. Kister, St. Charles, Vice-President; and Dr. L. E. Belding, St. Charles, Secretary-Treasurer.

South Central Counties Medical Society has elected the following officers: Dr. A. H. Thornburgh, West Plains, President; Dr. W. T. Herron, Houston, Vice-President; and Dr. A. C. Ames, Mountain Grove, Secretary-Treasurer.

The Jackson County Medical Society has moved its executive offices to a ten-room suite, 610 Argyle Building, Kansas City.

Dr. Carl F. Vohs, St. Louis, was elected President of the Northwest Regional Conference held in Chicago in February.

Dr. Robert Wilson Bartlett, St. Louis, and Miss Louise McGehee, of Memphis, Tennessee, were married January 5.

DEATHS

Dr. William Arthur Atkins, Rogersville, aged 59, died December 21 of coronary thrombosis.

Continued on page 40

THE JEFFERSON MEDICAL COLLEGE of PHILADELPHIA

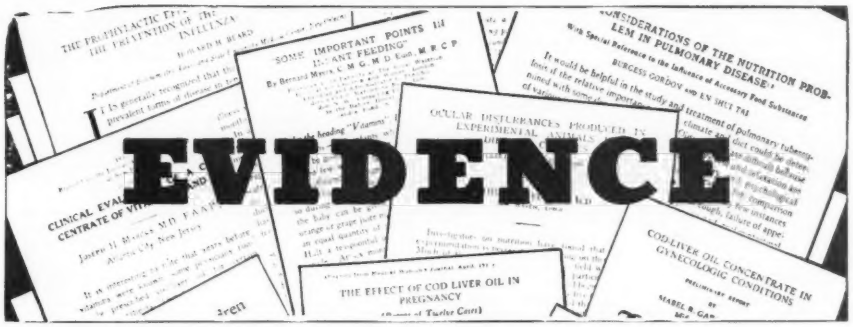
THE ONE HUNDRED AND FOURTEENTH ANNUAL SESSION BEGINS SEPTEMBER 20, 1938, AND ENDS JUNE 2, 1939.

FOUNDED 1825. A Chartered University Since 1838. Graduates number 16,313.

FACILITIES: New College Building; Curtis Clinic; Daniel Baugh Institute of Anatomy; Department for Diseases of the Chest; Jefferson Hospital; teaching museums and free libraries; instruction privileges in four other hospitals.

ADMISSION: A college degree based on four years of college work including certain specified science and language courses is required.

ROSS V. PATTERSON, M.D., Dean.


EVIDENCE
THE PROPHYLACTIC FEED IN THE PREVENTION OF INFLUENZA
SOME IMPORTANT POINTS IN INFANT FEEDING
CONSIDERATIONS OF THE NUTRITION PROBLEM IN PULMONARY DISEASE
OCULAR DISTURBANCES PRODUCED IN EXPERIMENTAL ANIMALS
CLINICAL EVALUATION OF VITAMIN CONCENTRATE
THE EFFECT OF COD LIVER OIL IN PREGNANCY
COD LIVER OIL CONCENTRATE IN GYNECOLOGIC CONDITIONS

An ever-increasing amount of evidence testifies not only to the importance of the cod liver oil vitamins in clinical practice, but also to the necessity for presenting these vitamins in standardized, easily administered dosage forms.

Bibliographic Evidence

Medical literature has emphasized and re-emphasized the necessity for providing the vitamins A and D in adequate unitage, and readily acceptable form, particularly during the periods of growth, pregnancy, lactation and convalescence.

Laboratory Evidence

Carefully controlled bioassay and spectrophotometric methods of standardization are carried out to assure a uniform A and D potency in White's Cod Liver Oil Concentrate 100 times greater than that of cod liver oil*. These are the natural vitamins of cod liver oil—not fortified by synthetic substances.

Clinical Evidence

The final test—its value in daily practice. Widespread acceptance of White's Cod Liver Oil Concentrate by the medical profession is obvious in the fact that today White Laboratories, Inc. is one of the world's largest users of cod liver oil for pharmaceutical purposes. Ethically promoted—not advertised to the public.

3 Palatable Forms

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EACH TABLET EQUALS 1 TEASPOONFUL
EACH CAPSULE EQUALS 4½ TEASPOONFULS

ACCEPTED AMERICAN MEDICAL ASSN.

Continued from page 38

Dr. Will P. Bradley, Windsor, aged 68, died November 1 of carcinoma of the sigmoid.

Dr. Richard Henry Fuhrmann, St. Louis, aged 57, died December 21 of carcinoma of the right lung.

Dr. Henry M. Lint, St. Joseph, aged 74, died November 20.

Dr. Frederick McKendrie Lowe, Kansas City, aged 66, died December 20 of peritonitis and carcinoma of the cecum.

Dr. Louis Laurenzana, Kansas City, aged 67, died December 11 of a heart attack.

Dr. Clarence Martin, St. Louis, aged 60, died December 7 following a gallbladder operation.

Dr. S. Edgar Miles, St. Louis, aged 81, died October 26.

Dr. James W. Mott, Poplar Bluff, aged 74, died November 15 of bronchopneumonia.

Dr. Leo Gregory McKellops, Neosho, aged 69, died November 17 of diabetes mellitus.

Dr. Reinhold Passler, St. Louis, aged 75, died November 27 of septic myocarditis following pyonephritis.

Dr. Robert Warren Smart, Aurora, aged 60, died November 10 of chronic myocarditis and hypertension.

Dr. A. W. Thompson, Kansas City, aged 65, died November 17 of cerebral hemorrhage.

Dr. George C. Thompson, Kansas City, aged 69, died in November.

Dr. Abraham Weinberg, Kansas City, aged 49, died November 30 of arteriosclerosis, heart disease and nephritis.

NORTH CAROLINA

At the meeting of the Tri-State Medical Association of the Carolinas and Virginia, held in Asheville, Dr. J. F. Highsmith, Fayetteville, was elected President; Dr. A. E. Baker, Charleston, South Carolina, President Elect; and Dr. J. M. Northington, Charlotte, Secretary-Treasurer, re-elected. The Vice-Presidents elected are: Dr. Wright Clarkson, Petersburg, Virginia; Dr. W. L. Pressly, Due West, South Carolina; and Dr. Charles A. Tinsley, Asheville. Charleston, South Carolina, was chosen as the 1939 meeting place.

The Southeastern Obstetrical and Gynecological Society held its organization meeting at Charlotte, February 4-5, and elected as officers: Dr. J. R. McCord, Atlanta, Georgia, President; Dr. R. E. Seibles, Columbia, South Carolina, Vice-President; and Dr. R. A. Ross, Durham, Secretary-Treasurer.

Rockingham County Medical Society has elected the following officers: Dr. A. M. Cox, Madison, President; Dr. P. S. Watson, Madison, Vice-President; Dr. E. E. Reynolds, Mayodan, Secretary-Treasurer.

Halifax County Medical Society has elected the following officers: Dr. P. W. Joyner, Enfield, President; Dr. F. W. M. White, Halifax, Vice-President; Dr. R. S. McGeachey, Weldon, Secretary-Treasurer.

Directors of the Johnston County Hospital for this year are: Drs. A. H. Rose, M. Hinnant, R. P. Holding, W. M. Gaskins, V. A. Divisian, Rufus Creech and W. J. Huntley.

A committee has been named to seek funds for construction of a new wing to the North Carolina Baptist Hospital, Winston-Salem.

The Duke University Medical Society was organized in December to hold monthly meetings during the academic year for discussion of current problems.

A new twenty-eight bed hospital for the treatment of tuberculosis was opened at Tarboro in December. It was built by Edgecombe County with the assistance of PWA funds. Dr. Lorenzo L. Parks, Health Officer of the Edgecombe-Greene Health District, Tarboro, is Medical Director.

Dr. Joseph R. Blalock, formerly of the staff of the New York State Psychiatric Institute and Hospital, has been appointed Superintendent of the Southwestern State Hospital, Marion, to succeed Dr. George A. Wright, who resigned.

The Wesley Long Hospital, Greensboro, has elected to its medi-

Continued on page 42

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FOR RENT OR SALE—X-Ray, diagnostic and therapy plant, including diathermy and quartz lamp. This equipment will be sold for $1,000.00, or it may be rented for $60.00 per month. Rental includes rent of Therapy Department in East Alabama Hospital for indefinite period. Very good field for work. Write Dept. BSB, care JOURNAL.

WANTED—Sixty-year-old firm marketing a small line of ethical specialties seeks the services of a capable detail man to handle its affairs in eastern Texas and Oklahoma. Prefer resident of Dallas. State full details of experience. Box E, care JOURNAL.

WANTED—Thoroughly trained men in orthopedics and eye, ear, nose and throat, preferably men recently graduated from A-1 school and just finishing residences, to become associated with clinic in South Florida. Address C. E. T., care JOURNAL.

POSITION DESIRED—Fully qualified physician desires permanent hospital staff appointment or group clinic appointment with practice limited to anesthesia. Address inquiries to Dept. 9, care Southern Medical Association, Birmingham, Alabama.

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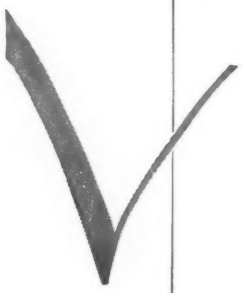

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Please send copies of the Dryco Infant Feeding Schedule.
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Continued from page 40

tal staff Dr. Samuel F. Ravenel, President; Dr. Henry Sikes, Vice-President; and Dr. E. D. Apple, Secretary.

Dr. Samuel F. Ravenel, Greensboro, was presented a silver plaque by the President of the Guilford County Medical Society, Dr. Russell O. Lyday, for having accomplished most as a member of the Society in the past year.

Dr. Loren Wallin, formerly of Sparta, Georgia, has been appointed Health Officer of Anson County, a new health unit.

Dr. Clifford W. Lewis, Beaufort, has been elected President of the local Chamber of Commerce.

Dr. James H. Bunn, Jr., formerly of Henderson, has been appointed head of a new health unit in Johnston County, with headquarters in Smithfield.

Dr. W. T. Rainey, Fayetteville, is the new President of the Cape Fear Area Council of the Boy Scouts of America.

Dr. Paul W. Sanger announces the opening of offices in the Medical Arts Building, Charlotte, for the practice of general surgery.

DEATHS

Dr. Norfleet Mann Gibbs, New Bern, aged 65, died December 25 of arteriosclerosis and hypertension.

Dr. Isham Faison Hicks, Dunn, aged 61, died January 21.

Dr. Wilson C. Martin, Mocksville, aged 72, died December 5 of carcinoma of the sigmoid.

Dr. Frederick A. Whitaker, Kinston, aged 87, died November 2 of chronic myocarditis and nephritis.

OKLAHOMA

At a meeting of the Board of Regents of the University of Oklahoma held January 3, 1938, upon the recommendation of the faculty of the medical school the pre-medical educational requirements for admission to the School of Medicine of the University of Oklahoma were raised from two years to three years, or ninety (90) college credit hours, exclusive of physical education or military science. The new requirements will become effective with the freshman class to enter the medical school in September, 1939.

Hughes County Medical Society has elected the following officers: Dr. W. L. Taylor, Holdenville, President; Dr. R. B. Ford, Holdenville, Vice-President; and Dr. Imogene Mayfield, Holdenville, Secretary-Treasurer.

Muskogee County Medical Society has elected the following officers: Dr. Finis W. Ewing, President; Dr. Ira C. Wolfe, Vice-President; and Dr. Shade D. Neely, Secretary-Treasurer, all of Muskogee.

Payne County Medical Society has elected the following officers: Dr. E. M. Harris, Cushing, President; Dr. P. M. Richardson, Cushing, Vice-President; and Dr. John W. Martin, Cushing, Secretary-Treasurer.

Pittsburg County Medical Society has elected the following officers: Dr. Allen R. Russell, President; Dr. Floyd T. Bartheld, Vice-President; and Dr. E. D. Greenberger, Secretary, all of McAlester.

Southeastern Oklahoma Medical Association has elected the following officers: Dr. E. H. Shuller, McAlester, President; Dr. W. Keiler Haynie, Durant, Vice-President; and Dr. John A. Haynie, Durant, Secretary-Treasurer.

Tulsa County Medical Society has elected the following officers: Dr. M. J. Searle, President; Dr. A. Ray Wiley, President-Elect; Dr. P. P. Nesbitt, Vice-President; and Dr. Roy L. Smith, Secretary-Treasurer, all of Tulsa.

Woods County Medical Society has elected Dr. Arthur E. Hale, Alva, President, and Dr. O. E. Templin, Alva, Secretary.

Dr. R. H. Lynch, Hollis, has been appointed County Health Superintendent of Harmon County.

Dr. B. J. Cordonnier, Okeene, has been doing postgraduate work at the Augustana Hospital in Chicago.

Dr. E. S. Kilpatrick has moved from Elk City to Leedey, where he will establish a private practice and hospital.

Dr. J. M. Pemberton has moved from Oklahoma City to Okemah.

Dr. Huston K. Spangler, formerly Assistant Superintendent of the Worcester, Massachusetts, City Hospital, has been appointed Superintendent of Valley View Hospital, Ada, upon its completion.

DEATHS

Dr. H. A. Harris, McAlester, died in January.

Dr. Charles Caton, Wynona, aged 62, died January 3.

Dr. John William Padberg, Choctaw, aged 67, died November 15.

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SOUTH CAROLINA

The Edisto Medical Society, composed of Bamberg, Calhoun and Orangeburg Counties, elected the following officers: Dr. C. I. Goodwin, Holly Hill, President; Dr. J. W. Harter, Orangeburg, Vice-President; and Dr. H. M. Eargle, Orangeburg, Secretary-Treasurer.

Florence County Medical Society has elected the following officers: Dr. James McLeod, President; Dr. L. B. Salters, Vice-President; and Dr. James A. Bradley, Secretary-Treasurer, re-elected, all of Florence.

Laurens County Medical Society has elected the following officers: Dr. F. K. Shealey, Clinton, President; Dr. M. B. Nickles, Laurens, Vice-President; and Dr. J. L. Fennel, Waterloo, Secretary-Treasurer.

Lexington County Medical Society has elected the following officers: Dr. F. L. Geiger, Columbia, President; Dr. A. T. Hutto, Pelion, Vice-President; and Dr. J. H. Mathias, Lexington, Secretary-Treasurer.

The Columbia Hospital, Columbia, has elected Dr. Izard Josey Chief of Staff; Dr. F. E. Zemp, Vice-Chief; and Dr. J. M. Davis, Secretary. The Executive Committee is composed of Dr. A. T. Moore, Dr. L. E. Madden and Dr. J. E. Boone.

Dr. O. E. Herndon, Chief Medical Officer of the Veterans' Hospital, Columbia, has been transferred to Tuscaloosa, Alabama. Dr. Henry Tobias, Batavia, New York, will fill Dr. Herndon's place.

Dr. H. A. Gross, Barnwell, is County Physician for Barnwell County.

Dr. F. C. Locke, who has been Chief of the Medical Service at the Veterans' Hospital, Columbia, has been transferred to Pittsburgh, Pennsylvania.

Dr. John M. Preston and Mrs. Lula W. Ellis, both of Lancaster, were married December 4.

Dr. Henry Young Harper and Miss Sara Vandiver, both of Anderson, were married February 19.

Continued on page 44

MOST POTENT ESTROGENIC FACTOR

in PROGYNON-DH and PROGYNON-B

. . . these preparations have proved valuable in the economic management of estrogenic hormone deficiencies, such as:

MENOPAUSAL SYMPTOMS	FUNCTIONAL DYSMENORRHEA
NAUSEA OF PREGNANCY	GONORRHEAL VAGINITIS
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Schering Corporation was the first to perfect the highly potent dihydro form of the follicular hormone (estradiol or dihydroxyestrin). Estradiol is the active substance in Progynon-DH tablets, suppositories and ointment, and as a benzoate in Progynon-B ampules. Research indicates that estradiol may be considered the true ovarian follicular hormone and many times more active than estrone (theelin or ketohydroxyestrin), one of the forms in which the estrogenic hormone is excreted in human urine.

To facilitate accurate dosage, Progynon-DH and Progynon-B in oil are supplied in several strengths, the latter material as high as 10,000 Rat Units (50,000 International Units) per 1 cc. ampule. Only with Progynon-B is it possible to administer such concentration in a single 1 cc. dose. This high concentration is of definite advantage in cases of extreme follicular hormone deficiency.

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Progynon-B* in oil **– 500 Rat Units, 1000 Rat Units, 2000 Rat Units, 10,000 Rat Units per ampule of 1 cc. size.** ***Progynon-DH* Tablets*** **– 50, 200 and 600 Active Biological Units per tablet.** ***Progynon-DH* Vaginal Suppositories*** **– 250 Rat Units per juvenile size suppository; 250 and 2500 Rat Units per adult size suppository.** ***Progynon-DH Lanol**** **– 200 and 1000 Rat Units per gram, in 50 gram jars.**

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BLOOMFIELD, NEW JERSEY

Continued from page 42

Dr. Isaac Hayne, Congaree, and Miss Susie Stephenson, Denmark, were married February 8.

DEATHS

Dr. N. Yancey Alford, Wisacky, aged 75, died November 6.

Dr. William Gordon Bodie, Wagener, aged 45, died December 31 of injuries received when struck by an automobile.

Dr. Kivy I. Pearlstine, Charleston, aged 53, died November 25 of coronary thrombosis.

Dr. Franklin Frost Sams, Charleston, aged 70, died November 2.

Dr. Julius Heyward Taylor, Columbia, aged 61, died January 31.

TENNESSEE

Fayette-Hardeman County Medical Society has elected the following officers: Dr. F. K. West, Rossville, President; Dr. B. F. McAnulty, Bolivar, Vice-President; and Dr. Wiley D. Lewis, Western State Hospital, Secretary.

Five-County Medical Society (Putnam, Cumberland, Jackson, Overton and White) has elected the following officers: Dr. Harlan H. Taylor, Cookeville, President; Dr. V. O. Bertram, Crossville, Vice-President; and Dr. Fred Terry, Cookeville, Secretary-Treasurer.

Dr. Clarence E. Gillespie, Memphis, and Miss Dixie Ruth Denton, Slat Spring, Mississippi, were married December 8.

DEATHS

Dr. Gilbert Taylor Abernathy, Paris, aged 78, died December 27 of injuries received when struck by an automobile.

Dr. Edward Chambers, Millington, aged 65, died December 22 of pneumonia.

Dr. M. G. Herrell, Powell Station, died February 4.

Dr. Walter J. Miller, Johnson City, aged 82, died recently.

Dr. Alpheus Leslie Sharber, Nashville, aged 59, died November 30.

TEXAS

Anderson-Houston-Leon Counties Medical Society has elected the following officers: Dr. Paul B. Stokes, Crockett, President; Dr. E. P. Powell, Centerville, Vice-President; and Dr. John T. Humphries, Palestine, Secretary-Treasurer.

Brown-Mills-San Saba Counties Medical Society has elected the following officers: Dr. J. M. Campbell, Goldthwaite, President; Dr. W. S. Pence, San Saba, Vice-President; and Dr. J. M. Horn, Brownwood, Secretary-Treasurer, reelected.

Childress-Hollingsworth-Hall Counties Medical Society has elected the following officers: Dr. E. W. Moss, Wellington, President; Dr. C. E. High, Wellington, Dr. J. D. Michie, Childress, and Dr. H. F. Schoolfield, Memphis, Vice-Presidents; and Dr. D. C. Hyder, Memphis, Secretary-Treasurer, reelected.

Dallas County Medical Society has elected the following officers: Dr. Lee Hudson, President; Dr. Marvin D. Bell, Vice-President; and Dr. W. W. Fowler, Secretary-Treasurer, reelected, all of Dallas.

Denton County Medical Society has elected the following officers: Dr. Bert E. Davis, Denton, President; Dr. M. L. Hutcheson, Denton, Vice-President; and Dr. John M. Hooper, Denton, Secretary-Treasurer.

Gonzales County Medical Society has elected the following officers: Dr. W. T. Dunning, Gonzales, President; Dr. A. B. Parr, Gonzales, Vice-President; and Dr. L. J. Stahl, Gonzales, Secretary-Treasurer, reelected.

Hardin-Tyler Counties Medical Society has elected the following officers: Dr. W. H. Beasley, Silsbee, President; Dr. I. R. Fowler, Silsbee, Vice-President; and Dr. John H. Hunter, Acol, Secretary-Treasurer, reelected.

Harrison County Medical Society has elected the following officers: Dr. Ray H. Carter, Marshall, President; Dr. Frank V. Mondrik, Longview, Vice-President; and Dr. Samuel W. Tenney, Secretary-Treasurer.

Hunt-Rockwell-Kains Counties Medical Society has elected the following officers: Dr. J. C. Cheatham, Wolfe City, President; Dr. P. W. Pearson, Emory, Vice-President; and Dr. W. P. Hilips, Greenville, Secretary, reelected.

Jasper-Newton Counties Medical Society has elected the following officers: Dr. W. F. McCreight, Kirbyville, President; and Dr. W. R. Worthey, Call, Secretary-Treasurer.

Kaufman County Medical Society has elected the following officers: Dr. G. H. Alexander, Terrell, President; Dr. H. S. Taylor, Kaufman, Vice-President; and Dr. John C. Aarni, Forney, Secretary-Treasurer.

Liberty-Chambers Counties Medical Society has elected the following officers: Dr. R. H. Engledow, Anahuac, President; Dr. A. L. Delaney, Liberty, Vice-President; and Dr. E. J. Tucker, Liberty, Secretary-Treasurer.

Orange County Medical Society has elected the following officers: Dr. L. O. Thompson, President; Dr. H. W. Pearce, Vice-President; and Dr. F. W. Lawson, Secretary-Treasurer, all of Orange.

Northeast Texas District Medical Society has elected the following officers: Dr. M. A. Walker, Paris, President; Dr. J. W. Ward, Greenville, Vice-President; and Dr. R. S. Usry, Dallas, Secretary-Treasurer, reelected.

The Hotel Dieu Hospital staff, Beaumont, has elected the following officers: Dr. Taylor Walker, President; Dr. S. J. Lewis, Secretary; and Drs. T. Alvin Fears, Stuart T. Wier and H. Grady Bevil, members of the Executive Committee.

The Dallas Methodist Hospital staff, Dallas, installed the following officers: Dr. Wayne T. Robinson, President; Dr. B. E. Greer, Vice-President; Dr. B. E. Park, Secretary; and Drs. George C. Kindley and J. H. McGuire, Councilors.

Bethania Hospital staff, Wichita Falls, has elected the following officers: Dr. William E. Rosenblatt, President; Dr. L. B. Holland, Vice-President; Dr. B. R. Collins, Secretary; Dr. C. W. Stephenson, Assistant Secretary; and Drs. R. L. Hargraves, J. A. Heyman and J. E. Kanatser, members of the Executive Committee.

Hendrick Memorial Hospital staff, Abilene, has elected the following officers: Dr. J. M. Alexander, President; Dr. W. V. Ramsey, Vice-President; and Dr. W. B. Adamson, Secretary.

St. Therese Hospital staff, Beaumont, has elected the following officers: Dr. Ernest Robertson, President; Dr. Taylor Walker, Vice-President; and Dr. G. B. Stephenson, Secretary.

The Northeast Texas Hospital Association was organized in December at Longview and the following officers elected: Dr.

Continued on page 46

To Assure Quick Dependable Response
Discriminating Physicians are Prescribing
the easily soluble
DUBIN AMINOPHYLLIN
THEOPHYLLINE-ETHYLENEDIAMINE
American Made from American Materials
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Puritan Portable OXYAERATOR

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THIS UNIT IS . . . .

COMPLETE—All necessary equipment furnished and self-contained for the nasal administration of Oxygen therapeutically. Delivered to you completely assembled.

PORTABLE—Weighs only approximately 11 lbs.

COMPACT—Only 7″ high, 6½″ wide, 6″ deep.

PRICE—Each Complete:

Less cylinder truck and cylinder.....$70.00
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A hot drink before retiring is an aid in promoting restful sleep. Horlick's Malted Milk, hot, has special advantages for this purpose in that it is pleasant in flavor, easily and quickly digested, bland and nourishing.

Horlick's Malted Milk Tablets, to be dissolved in the mouth, are convenient to keep at hand, offering concentrated nourishment, quickly assimilated at any time of the day or night.

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RACINE, WIS.

Continued from page 44

L. N. Markham, Longview, Chairman; Dr. Sartin Ambrose, Tyler, Vice-Chairman; and Miss Mae Kennedy, Paris, Secretary.

The new Jefferson Davis Hospital, Houston, constructed at a cost of $2,500,000, was opened in January. It has not yet been determined what disposition shall be made of the old hospital plant.

A new dormitory ward building is being constructed as a part of an extensive building program at the Rusk State Hospital, Rusk, which will cost $115,000. A total cost in connection with the improvements for 1938 is estimated at $417,000 for buildings and equipment.

The Alexander Hospital, Spur, was opened January 5. It was built by Dr. R. L. Alexander largely to take care of maternity cases, although general cases will probably be received later.

The Callan and Wilkinson Clinic, being built by Drs. C. U. Callan and R. T. Wilkinson, is now under construction at Rotan, and will cost approximately $25,000.

The Donop Clinic and Hospital, constructed at Fredericksburg by Dr. P. T. Donop at a cost of $60,000, was opened December 26. The hospital will be operated on the closed staff basis.

Dr. Jack C. Harper, formerly of Dallas, has been appointed Director of the Gregg County Health Unit.

Dr. William H. Bradford, Dallas, was recently elected President of the Dallas Pediatric Society.

Dr. Emory D. Hollar was recently elected Health Officer of Wilbarger County.

Dr. C. F. Neuville, Nacogdoches, was recently appointed local oculist and aurist for the Southern Pacific Railroad.

Dr. F. Fred Freeland has moved from Sulphur Springs to Abilene.

Dr. D. B. Kantor has moved from McAllen to Fairbury, Nebraska.

Dr. H. F. Laramore has moved from Dallas to Atlanta, Georgia.

Dr. A. L. McElroy has moved from Aspermont to Hamlin.

Dr. C. H. Miller has moved from Crane to Lubbock.

Dr. C. F. Neuville has moved from Commerce to Nacogdoches.

Dr. Lewis Silver has moved from Terrell to Dallas.

Dr. Louis E. Silverthorn has moved from CCC Camp Goliad to Fort Sam Houston.

Dr. Marcellus Walker, Jr., Paris, and Mrs. Clara Billingsley McCain were married recently.

Dr. Joe W. Howze, Pampa, and Miss Ann Pittman, Corpus Christi, were married in November.

Dr. Robert Harris, Pilot Point, and Miss Virginia White, Durham, North Carolina, were married December 18. Dr. Harris is now a resident physician at the Methodist Hospital, Fort Worth.

Deaths

Dr. Harvey Oliver Brannon, Fort Worth, aged 55, died December 7 of coronary thrombosis, hypertension and myocarditis.

Dr. George Malcolm Graham, Austin, aged 51, died December 25 of encephalitis.

Dr. Samuel Elbert Lundy, Fort Worth, aged 58, died December 11 of coronary occlusion.

Dr. Margarito Montemayor, San Antonio, aged 61, died November 9 of coronary sclerosis.

Dr. Felix Summerfield Martin, Beaumont, aged 67, died December 23 of coronary thrombosis.

Dr. Thomas R. Ogden, Jasper, aged 73, died November 29 of carcinoma of the stomach.

Dr. James Augustus Pickett, El Paso, aged 56, died January 27 of peritonitis.

Dr. Charles L. Root, Colorado, aged 67, died December 10 of heart disease.

Dr. W. W. Samuell, Dallas, aged 59, died December 12 of coronary occlusion.

VIRGINIA

The Medical Society of Virginia will hold its next annual meeting at the Hotel Danville, Danville, October 4-6.

Alexandria Medical Society has elected Dr. Carson L. Fifer President and Dr. C. T. Arnette Secretary-Treasurer, both of Alexandria.

Lee County Medical Society has elected Dr. B. C. Grigsby, St. Charles, President; Dr. W. L. Griggs, Benedict, and Dr. J. G. McNeil, St. Charles, Vice-Presidents; and Dr. J. B. Munch, Pennington Gap, Secretary-Treasurer, reelected.

Wise County Medical Society has elected the following officers:

Continued on page 48

VITAMIN THERAPY

Takes an Important Step Forward

THE WAY in which the medical profession has ever kept abreast of scientific research in the important field of vitamins, has been a striking demonstration of its alertness to new concepts.

Following the discovery of vitamins by Dr. Funk in 1912, doctors everywhere were quick to seize on the first commercial concentrate of A and D, made available by Funk and Dubin in 1923. In following years, as new vitamins were discovered, they have been promptly added to the physician's armamentarium. Their influence on the modern development of nutritional science has been of the highest significance.

Today the history of vitamin therapy takes another important forward step with the recent discovery of the cooperative interdependence existing between vitamins and minerals. In Vi-Syneral, Funk and Dubin have made available a potent concentrate of the six known vitamins—A, B_1, B_2(G), C, D and E—fortified with eight essential minerals—calcium, phosphorus, iron, copper, manganese, iodine, magnesium and zinc.

The superior efficacy of this multiple vitamin-mineral concentrate over mere A-D, A-B-D-G, or even A-B-C-D-G preparations, has been strikingly demonstrated by laboratory tests by Dr. Walter H. Eddy at Columbia University.

Nor have physicians been slow to prescribe the latest scientific Funk-Dubin contribution as a means to corrective diet insurance, and as an aid in the recovery of optimum health and vitality. Clinical reports from all parts of the country attest to the gratifying response to this modern metabolic stimulant.

Vi-Syneral is available in Funk-Dubin balanced potencies for all age groups. The usual dosage is one vitamin and one mineral capsule daily, with any meal.

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The Original Multiple Vitamin-Mineral Concentrate

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makes available the therapeutic effect of standardized follicular hormones by oral administration, combined with the well known Hormotone endocrine formula. Each tablet contains ovarian follicular hormones therapeutically equivalent to 200 units (international assay). It is Enterosol Coated to prevent any destructive action of the digestive processes of the stomach.

Amenorrhea Menopause
Irregular Menstruation

Bottles of 40 tablets

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Newark, New Jersey

Continued from page 46

Dr. C. Robert Jones, Dorchester, President; Dr. A. W. Reeser, Appalachia, Dr. D. C. Keister, Osaka, and Dr. J. R. Massie, Norton, Vice-Presidents; and Dr. C. L. Harshbarger, Norton, Secretary-Treasurer, reelected.

The Neuropsychiatric Society of Virginia, at a meeting in Charlottesville, elected the following officers: Dr. Frank H. Redwood, Norfolk, President; Dr. H. C. Henry, Petersburg, Vice-President; and Dr. Thomas N. Spessard, Roanoke, Secretary-Treasurer.

Dr. Mary Harley, who was resident physician and Professor of Hygiene at Sweet Briar College, retired in June, 1936, and has since been devoting her time to travel and the study of anthropology. She has studied at the Universities of Hawaii and Pennsylvania and is now at the University of Virginia. Later she expects to study at Oxford, England, and at the University of Pretoria in South Africa.

Dr. S. D. Gardner, who has completed a postgraduate course at Johns Hopkins School of Hygiene and Public Health, has been reappointed Health Officer of the Valley Health District, with headquarters at Luray. Dr. Linwood Farley continues as Assistant Health Officer in this District.

Dr. J. M. Meredith, of the University of Virginia, has been appointed to the Committee on Relations with Other Educational Institutions by the President of the Associated Pennsylvania Clubs of the World, which will meet in Richmond in November.

The Second Vacation Postgraduate Cruise of the Seaboard Medical Association of Virginia and North Carolina will take place on Ship Reliance, leaving Norfolk June 11 and returning to Norfolk June 16. Dr. Clarence Porter Jones, Newport News, is Secretary-Treasurer.

Dr. Richard C. Neale, who has been connected with the Biochemical Research Foundation of the Franklin Institute in Philadelphia, has returned to Richmond and opened the Physicians' Service Laboratories.

Dr. Thomas L. Gemmill, for the past two years connected with the medical staff at Central State Hospital, Petersburg, is now located at Radford, where he is associated with Dr. W. B. Fuqua in the practice of general medicine.

Dr. Nelson Mercer, formerly of Richmond, but for the past year Resident Physician at Battle Hill Sanatorium, Atlanta, Georgia, is now located in Philadelphia as Resident Physician at the Home for Consumptives, Chestnut Hill, the oldest tuberculosis sanatorium in the United States.

Dr. John B. H. Bonner, Stony Creek, Health Officer of Sussex County, has been made Director of a new health district in Prince George County, with headquarters in Hopewell.

Dr. H. I. Slate, formerly of Cadiz, Ohio, has been appointed Resident Physician at the Southside Hospital, Farmville.

Dr. R. Campbell Manson announces his association with Dr. Thomas W. Murrell with offices at 17 East Grace Street, Richmond.

Dr. J. Newton Dunn has taken the office of the late Dr. John C. White to practice medicine at Blackstone.

Dr. James Davis Hagood, Clover, and Miss Wirt Jordan Irby, South Boston, were married January 19.

Dr. Herbert DeGrange Wolff, Jr., Alexandria, and Miss Anne Henderson Froehling, Richmond, were married February 12.

DEATHS

Dr. Charles Louis Rudasill, Richmond, aged 47, died January 13.

Dr. Robert Lee Seward, Isle of Wight, aged 75, died January 31.

WEST VIRGINIA

The annual midwinter meeting of the West Virginia Society of Industrial Physicians and Surgeons was held in Charleston, February 8.

The annual conference of County Medical Society Secretaries and Presidents was held in Charleston at the headquarters of the West Virginia State Medical Association, January 15.

Dr. Leon Dickerson has been appointed full-time Health Officer for Fayette County.

Dr. William H. Riheldaffer has been appointed District Health Officer of the Fifth District with headquarters at Romney.

Dr. William Earl McIlvaine has been appointed District Health Officer for the First District with headquarters at Sutton.

Dr. J. H. Crouch has been appointed District Health Officer for the Second District with headquarters at Lewisburg.

DEATHS

Dr. W. P. Beane, Keystone, aged 64, died February 16.

Dr. Lyndon Sewell Smith, Monongah, aged 65, died January 31.

In EMERSON'S C-G ALKALIZER,

the active ingredients, officially recognized, are combined in judicious proportion to quickly enrich the body with calcium and the blood with alkali.

CALCIUM GLUCONATE U.S.P.

Six teaspoonfuls of C-G Alkalizer will double the amount of calcium in average daily diet.

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URIC ALKALINITY LASTING FOUR TO SIX HOURS MAY BE INDUCED BY ONE DOSE REPEATED IN HALF HOUR.
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50 grains in every heaping teaspoonful of C-G Alkalizer for physiological alkalizing.

Not a laxative, C-G Alkalizer promotes elimination through intestines, kidneys and skin; also stimulates gastric function. Costs patients 25 to 35 per cent *less* than ordinary products of its type.

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is decidedly valuable in the care of expectant and nursing mothers, in the treatment of febrile diseases, convalescence, diarrhea, common cold, allergies — in acidosis and calcium depletion.

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His First Solid Food

The baby's first solid food always excites the parents' interest. Will he cry? Will he spit it up? Will he try to swallow the spoon? Far more important than the child's "cute" reactions is the fact that figuratively and physiologically this little fellow is just beginning to eat like a man.

PABLUM is now being fed to infants as early as the third or fourth month because it gets the baby accustomed to taking food from a spoon, but, most important, Pablum early adds essential food substances to the diet. Among these are vitamins B_1 and G and calcium and, perhaps most necessary, iron. Soon after a child is born its early store of iron rapidly diminishes, and as milk is poor in iron, the loss is not replenished by the usual bottle-formula. Pablum, therefore, fills a long-felt need, for it is so well tolerated that it can be fed even to the three-weeks' old infant with pyloric stenosis, and yet is richer than fruits, eggs, meats, and vegetables in iron. Even more significant, Pablum has succeeded in raising the hemoglobin of infants in certain cases where an iron-rich vegetable failed. Pablum is an ideal "first solid food."

Pablum consists of wheatmeal, oatmeal, cornmeal, wheat embryo, alfalfa leaf, beef bone, brewers' yeast, reduced iron, and sodium chloride.

Mothers appreciate the convenience of Pablum as it needs no cooking. Even a tablespoonful can be prepared simply by adding milk or water of any temperature.

Please enclose professional card when requesting samples of Mead Johnson products to cooperate in preventing their reaching unauthorized persons.

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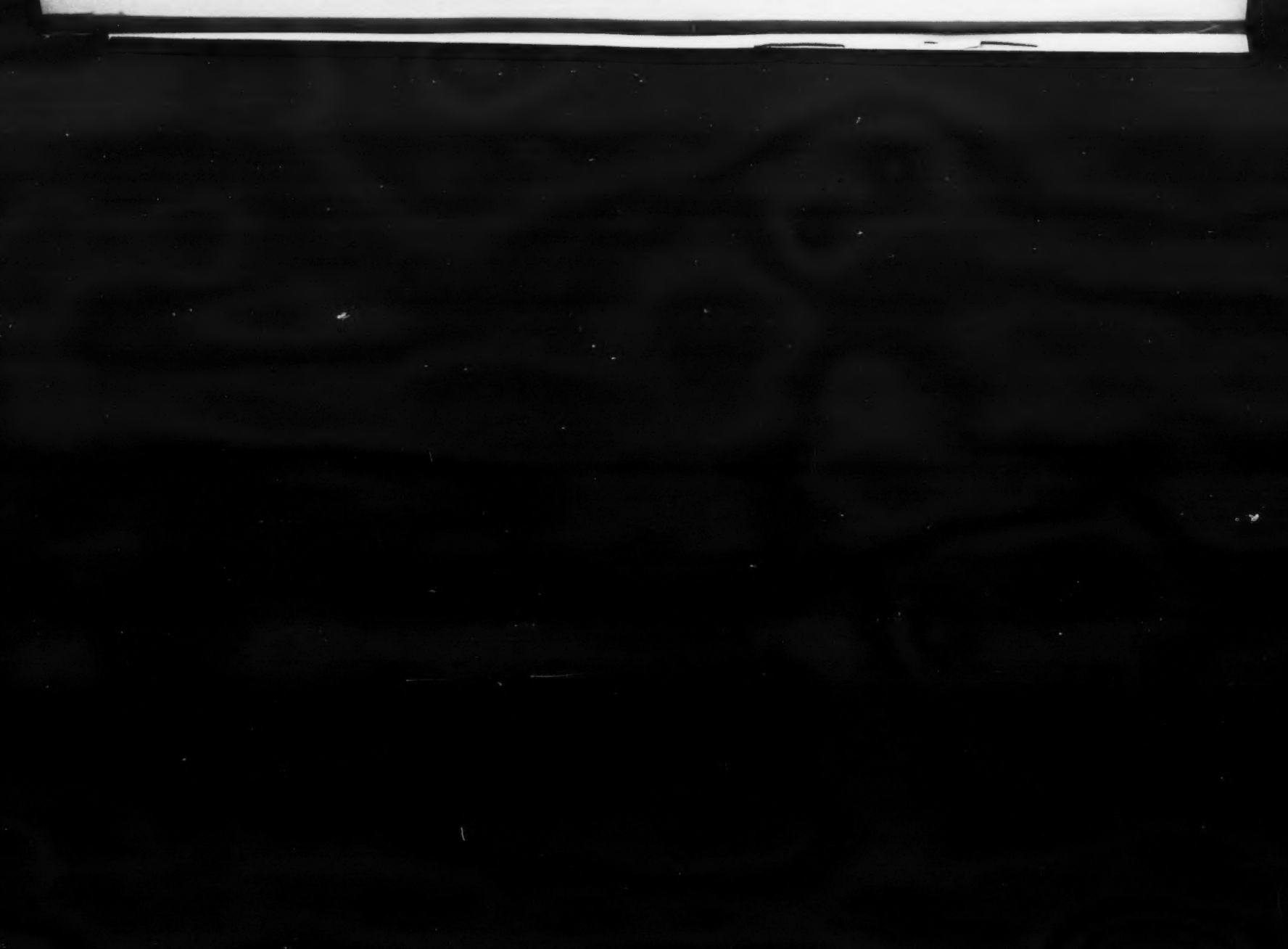


In the past a frequent complaint from mothers was the expense incurred when the large bottle of antiricketic was accidentally upset.

"Busy fingers" can't spill OLEUM PERCOMORPHUM

Even if the bottle of Oleum Percomorphum is accidentally tipped over, there is no loss of precious oil nor damage to clothing and furnishings. The unique Mead's Vacap-Dropper* is a tight seal which remains attached to the bottle, even while the antiricketic is being measured out. Mead's Vacap-Dropper offers these extra advantages also, at no increase in price:

Unbreakable

Mead's Vacap-Dropper will not break even when bottle is tipped over or dropped. No glass dropper to become rough or serrated.

No "messiness"

Mead's Vacap-Dropper protects against dust and rancidity. (Rancidity reduces vitamin potency.) Surface of oil need never be exposed to light and dust. This dropper cannot roll about and collect bacteria.

Accurate

This unique device, after the patient becomes accustomed to using it, delivers drops of uniform size.

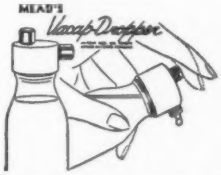
No deterioration

Made of bakelite, Mead's Vacap-Dropper is impervious to oil. No chance of oil rising into rubber bulb, as with ordinary droppers, and deteriorating both oil and rubber. No glass or bulb to become separated while in use.

**Supplied only on the 50 c.c. size; the 10 c.c. size is still supplied with the ordinary type of dropper.*

How to Use MEAD'S *Vacap-Dropper*

Remove both top and side caps. Wipe dropper tip. Regulate rate of flow by using finger to control entrance of air through top opening (see below). Oleum Percomorphum is best measured into the child's tomato juice. This is just as convenient and much safer than dropping the oil directly into the baby's mouth, a practice which may provoke a coughing spasm.



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Mapharsen (meta-amino-para-hydroxy-phenylarsine oxide hydrochloride) is available in single dose ampoules containing 0.04 and 0.06 Gm., each in individual packages with or without distilled water. It is also supplied in ten-dose ampoules, containing 0.4 and 0.6 Gm., for use by hospitals and clinics.

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